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THE
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ORIGINAL ARTICLES

THE THEORY AND TREATMENT OF DIABETES.¹

BY CARL VON NOORDEN, M.D.,

PROFESSOR OF THE FIRST MEDICAL CLINIC IN VIENNA, AUSTRIA.

I PROPOSE to present in broad outline the altered conditions of metabolism which occur in diabetes mellitus, and also to point out some of the indications for treatment which scientific investigations upon the metabolic disturbances have revealed.

The human body obtains its energy and nutrition from three types of foodstuffs: proteins, fats, and carbohydrates. For general purposes of work, warmth, and nutrition all three groups serve well; the muscular tissues are, however, more specific in their requirements. The working cells of the muscles do not utilize each type of foodstuff alike; they find the sugars the most useful for their energy production. It is possible, but not very probable, that they can use other materials for the same purpose, but this in too slight an extent to make the substitution of any practical importance, and we may, therefore, for the present leave this possibility out of our calculations.

As the working cells of the body use the sugars as their foodstuff and immediate source of energy, it is necessary that a mechanism should exist that renders the sugar always available for this purpose. The liver fulfils this function. The liver supplies the sugar in such a way that the arterial blood streaming to the tissues maintains an average sugar content of 0.75 to 0.85 sugar per 1000 parts of blood. The demands of the tissues for sugar

¹ Read before the Leland Stanford, Jr. University Medical School, San Francisco, and at the Johns Hopkins University, Baltimore. The questions mentioned in this paper are quoted in full in the author's book, *Modern Aspects of Diabetes Mellitus, its Theory and its Treatment*, New York.

vary to a large extent. During active muscular work they require four or five times as much sugar as when at rest. The liver responds to these needs by producing more or less sugar as occasion demands; the sugar requirements of the tissues determine the amount of sugar the liver is to produce. If this is put into commercial phraseology it might be said that supply and demand balance exactly. The maintenance of the sugar content of the blood is one of the most important functions of the liver. If the liver produces more sugar than the tissues require there is an abnormal amount of sugar present in the blood (hyperglycemia), and some of it escapes through the kidneys into the urine. On the other hand, if the liver does not manufacture sufficient sugar, the muscles suffer and signs of fatigue occur, because the working cells are insufficiently supplied with food. Such a condition appears during long-continued, strenuous muscular work. Then the need for sugar is so enormous that the liver is unable to meet the demand rapidly enough. The sugar content of the blood falls and severe fatigue and lack of energy appear.

In examining the sugar factories of the body—the liver cells—it will be found we have to deal with a complicated mechanism. It is well known that all the carbohydrates of the food are converted into sugar in the intestines and are carried to the liver in this form. It is only at certain times of the day when large quantities are being taken that carbohydrates are consumed and absorbed. If this quantity of carbohydrates simply passed through the liver there would result an excess of sugar in the blood; the sugar would not be completely used up, and a large part would be caught by the kidneys and excreted in the urine. This actually happens if healthy individuals eat large quantities of sugar. The condition thus produced has been termed “alimentary glycosuria.”

A special form of protection, however, exists for the prevention of this excessive flow of sugar into the blood after a large meal of carbohydrates. The liver takes up the sugar as soon as it arrives and stores it in its cells. In order that the easily soluble sugar may be retained in the cells it is instantly changed into an insoluble form known as “glycogen.” This glycogen is a reserve material. The liver conserves any overplus of sugar in this way so that any demands may be instantly met. In order to enter the circulation, however, the glycogen must be changed again into a soluble form, for as glycogen it cannot be transported *via* the blood to the muscles. To this end a ferment called diastase is provided. It is present in the liver in large quantities, although it occurs also in all the other organs and tissues. Diastase is widely distributed; it occurs in plants as well as in animals. It plays an important part in the nutrition of young plants in converting starch into sugar, just as it provides the blood with sugar for the muscles.

This storage of carbohydrates in the form of glycogen and the

further change of glycogen into sugar is not all that the liver can do. Human beings consume various kinds of foodstuffs, and they are not always able to obtain sufficient carbohydrates to meet the requirements of the body. Therefore, the organism is compelled to form sugar from other materials.

Albumins and fats are available for this purpose; proteins are considered as reserve materials of the first order and fats as reserves of a second order. The two substances play different parts. The albumins do not yield much sugar, but they act as strong irritants of the sugar-forming apparatus. When the liver cells break up the protein they are forthwith stimulated to form carbohydrate; the sugar formed from the albumin passes into the general circulation; thus it shares the same fate as sugar which as such reaches the liver with the food.

Fats act in another way. They form a rich source for carbohydrates. In those who consume small quantities of carbohydrates, and also in those who eat an average mixed diet, there is considerable formation of sugar from fat, for few people eat as much carbohydrate as their tissues require. Fat does not stimulate the sugar-forming apparatus in the liver; the hepatic cells use fat for this purpose only when other materials fail. Carbohydrates and proteins dictate the work of the sugar-forming apparatus; while fat, on the other hand, is the self-selected material of this apparatus.

It has been shown that the liver is the sugar-forming organ of the body. The diastatic ferment is a peculiarly active substance, which is not directly concerned with the demands of the tissues for sugar, and is somewhat of a menace to the glycogen content of the liver. If not checked it would furnish to the blood all the sugar-forming material that is brought to the liver, so that the blood would be either too rich or too poor in sugar. It is a fact that such an irregularity of the sugar factor occurs under certain conditions of disease. Healthy people, however, exhibit a perfect balance between sugar needs and sugar production; care is apparently taken that the diastatic ferment does not decompose more glycogen (that is, does not furnish more sugar) than is necessary to maintain the normal level of the sugar content of the blood. The exact chemical processes by which this is brought about are still unknown. It is not clear whether it is a physical or chemical property of the liver cells by which the action of the diastatic ferment is depressed or increased, nor do we know the nature of the signal which indicates to the liver cells the immediate needs of the tissues for sugar. However, many interesting facts have already been discovered.

One of the most important of them is the recognition that the liver is not so independent in its management of the sugar production as was at one time thought. There are at least two controllers which influence the intensity of the sugar-forming processes to a high degree; they both act as antagonists.

The pancreas is the first regulator to be considered. The blood from the pancreas passes to the liver and contains a specific product of the pancreatic cells (called an internal secretion), which exerts a retarding influence upon sugar production. If the pancreas be removed from the body this influence is also removed, and the amount of sugar produced in the liver is greatly and irregularly increased. Each type of material from which sugar can be produced becomes grist to the mill, and enormous quantities of sugar pass into the blood stream and raise the sugar percentage to an abnormal height, while a large amount escapes from the body in the urine. This is practically a severe type of diabetes. Clinical experiences show that diminished activity of the pancreas is the cause of a large number of cases of diabetes. This altered power of the pancreas is chiefly one of weakened function; there are not always anatomical changes in the structure of the gland. There are all grades of pancreatic insufficiency, and, dependent upon the condition of the pancreas, the disturbance of the regulation of the sugar processes is either intense or slight. It may vary considerably from time to time in the same case.

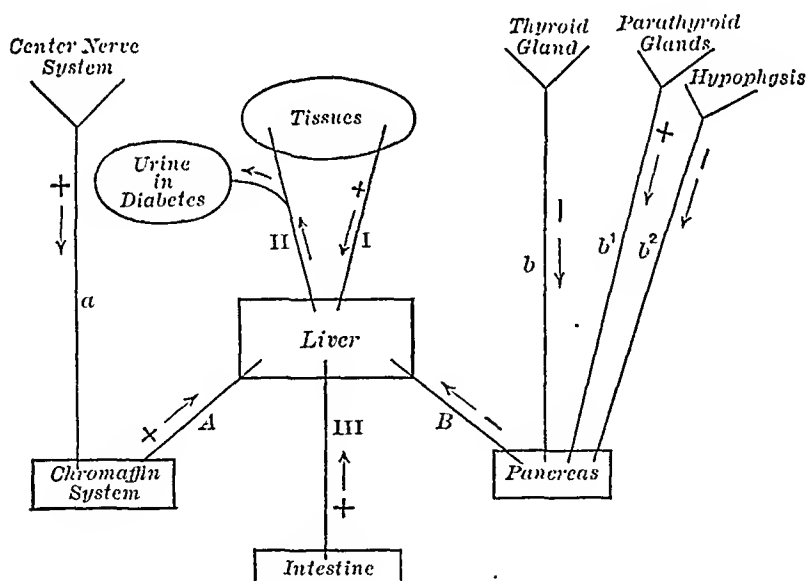
The other regulator is the suprarenal gland system. Minute quantities of adrenalin are being continually produced by this system and pass into the blood. This interesting substance possesses the property of exciting the sugar production in the liver to a high degree. As a rule the injection of about 1 milligram of adrenalin under the skin or into a vein will cause the excretion of sugar in the urine of an adult man within a quarter of an hour, which may continue for several hours. Experiments upon animals have shown that if the injections be repeated daily there is a regular response in the shape of urinary sugar, but the quantity gradually diminishes, and finally ceases to appear unless the dose of adrenalin be increased. The suprarenal, therefore, antagonizes the action of the pancreas so far as regards the regulation of sugar production. The one inhibits and the other stimulates the formation of sugar. The normal organism maintains its regulation of sugar production and output through the equilibrium that exists between these two agencies. Strong stimuli emanating from one organ may be compensated by increased action on the part of the other one. This has been proved by numerous experiments: In the beginning, injections of adrenalin, or an increased function of the gland itself, both excite the liver markedly. The pancreas, surprised, as it were, at the vigor of the irritant, is not able at the moment to avert the danger; it has to allow the undue increase of sugar production to have its sway. After some days, however, the repeated stimulation forces the pancreas to throw off its inertia and to oppose the action of the adrenalin. The antagonism between the two glands and their compensatory relations may be demonstrated by experiments.

However, neither of these two controllers of the sugar manu-

factories are able to act entirely independently. Their activities are influenced by forces external to themselves. This is especially the case with the suprarenals, which developmentally and functionally are directly under the control of the nervous system—the sympathetic nervous system acts as an intermediary between the central nervous system and the glands. The exact area of the nervous system which exercises this power is situated at the junction of the brain and the spinal cord. This well-known fact was discovered by Claude Bernard. The glycosuria which results from the puncture of Claude Bernard's centre in the medulla is due to the action of the central nervous system upon the suprarenal glands *via* the sympathetic nerves; adrenalin is at once formed in larger quantity, passes into the blood, and stimulates the sugar production in the liver. This "piqûre" glycosuria is practically the same as suprarenal glycosuria. It has been found, also, that nerve injuries of different kinds, and also many poisons, lead to the appearance of glycosuria. In all these instances it is a question of reflex or toxic irritation, which excites Claude Bernard's centre, with the subsequent excess formation of adrenalin and stimulation of the sugar-forming tissues. At the first appearance these observations seem to show that a considerable number of cases of diabetes are due to similar nervous causes (neurogenous diabetes). However, in spite of all this and many other findings it is still not yet clear whether there exists a chronic form of diabetes which only arises from neuropathic or suprarenal sources. There is no doubt but that the nervous system and the suprarenals play an important part in those acute rapid forms of glycosuria which are associated with psychical, nervous, cerebral irritations or with acute toxemias, and which often disappear entirely. They play also a definite part in chronic diabetes; cases are often seen in which the glycosuria increases as a result of nervous irritation or cerebral overstrain apart from any influence of the food consumed. In almost every case of diabetes it is possible to distinguish a nervous and an alimentary factor. However, the glycosuria may only be considered as purely neurogenous, when it is transitory and if it is perfectly independent of any foodstuff. But, if the glycosuria reappears after transitory psychical or nervous attacks, and if during these phases the composition of the food exerts any definite influence upon the appearance or disappearance of the glycosuria, then we may not regard the condition as a genuine neurogenous diabetes, but must think of some concurrent diminished activity of the pancreas. For the "nervosity," that is, the hypersensitiveness of the nervous centres and paths, does not alone suffice to explain the condition; otherwise, neurasthenics would, as a rule, show tendencies to glycosuria. This is, however, not the case; the greater number of neurasthenics are not glycosurics even if they present other signs of irritation of the sympathetic system.

Neither does the pancreas work independently: Its energies may be influenced from outside. We now come in contact with the properties of the thyroid gland. The thyroid secretes chemical substances which it passes into the blood. These are the same substances which are sometimes used in obesity. An overproduction of the thyroid secretion paralyzes the action of the pancreas; pancretic vigilance over the hepatic functions becomes diminished, and so in cases of voluntary thyroidal overproduction (Graves' disease) or after administration of thyroid extract the urine may contain sugar. For this reason great care should be used in employing thyroid extract. On the other hand, the pancreas becomes more energetic and powerful when the thyroid gland secretion is diminished, as in myxedema, cretinism, and thyroid ablation. In these diseases, no matter whether large amounts of sugar are given or the suprarenals send out increased stimuli, glycosuria does not occur. The pancreas reacts most probably to other influences also, but accurate information about these is not yet available.

We see, therefore, that the work of the sugar factory is a complicated process. Perhaps the mechanism may be put more clearly in the form of the accompanying diagram.



The manufactory for sugar is the liver, and the liver cells constitute the working department.

The important claims that *determine* the amount of the sugar production arrive from other organs and tissues, especially from the muscles (path *I*). The greater the consumption of sugar the stronger will be the claiming impulse, and an amount of sugar sufficient

to meet the demand will pass into the blood (path *II*). This is normally the only influence which induces the liver to raise its output.

However, along path *III* stimuli will also pass. This path represents the blood streaming into the liver from the intestinal wall, and carrying carbohydrates and the products of protein digestion. The quantity of these materials varies according to the type and composition of the food. So long as the manufacture of sugar is well under control the effect of this form of stimulus is not to induce a liberal outpouring of sugar into the general blood stream, but to form glycogen. This glycogen is then stored until it is reconverted into sugar at the request of the tissues, and travels along path *II* to the muscles, etc.

In order to maintain the excitability of the sugar manufactories at the proper intensity the two controlling factors come into play. The pancreas, which depresses the excitability, sends its secretion along path *B*, while the suprarenals, which increase the excitability, distribute their secretion along path *A*. This conjoined action serves to keep the process in equilibrium.

Both these controlling glands are in turn influenced by other organs—the pancreas through the thyroid gland path (*b*) and the suprarenal through the nerve paths (*a*). The diagram shows still other influences (path *b*¹ and *b*²); their existence is most probable, but their origin is undetermined. They seem to be subordinate in importance and action.

A consideration of the diagram and its explanation should lead to the conclusion that the excretion of sugar in the urine is not indicative of one disease alone. Of course, under all circumstances the glycosuria is a sign of increased production of sugar and an excess of sugar in the blood stream. Even if only traces of sugar are found in the urine it is evident there is an excess present in the blood.

The cause of the disturbance may be found in various places, but in the case of real diabetes several sources are of unequal importance.

1. Primary disease of the liver itself: This in reality plays a subordinate role. In some diabetics the liver is enlarged, but it is an hypertrophy resulting from overwork; the cells themselves are healthy. In primary disease of the liver, glycosuria is the exception, not the rule. If disease of the liver and diabetes occur in one and the same individual the two conditions appear independently.

2. Primary anomaly of the instreaming impulse along path *I*, that is to say, a demand for more than the actual needs of the tissues: This is theoretically possible. It plays an undoubted part in the form of diabetes due to phloridzin poisoning. This is, however, of experimental interest only. Such an intoxication does not throw any light upon the etiology of human diabetes, and

there is not a symptom indicating that overpowering impulses along path I may start human diabetes.

3. There may be an increased flow of sugar from the intestine along path *III*, which gives the glycogen-forming function of the liver too much to do and the untransformed sugar passes into the blood (transitory alimentary glycosuria). The normal powers controlling the sugar-producing factories are so high, however, that under ordinary conditions only an excessive quantity of sugar is too much for them, and some escapes into the blood stream. Should sugar appear in the urine of an adult upon an average sugar and starch diet it would be wrong to regard it as a physiological or harmless glycosuria. On the contrary, it should be regarded as an indication of a disturbed sugar mechanism and a slight form of diabetes. I mention this intentionally, because the term "alimentary glycosuria" has led to regrettable and costly errors. With this term many doctors console their patients, and many patients comfort themselves, especially if the glycosuria occurs only occasionally, and then disappears for a while in spite of liberal intake of carbohydrates. Such a fluctuation of the condition is not an exception in the early stages of diabetes; in fact, it is rather the rule than otherwise. This is the stage, moreover, in which rigorous treatment should be undertaken, for at this stage diabetes may often be cured. If the warning signal is not observed, the disease, in the majority of cases, progresses consistently, and then it is too late to realize that the consolation was ill-founded, and that in the past the patient has wasted both time and opportunity.

4. The anomalies connected with path *A* have already been stated. The disease may be in the suprarenal itself or in the course or head station of the line *a*; disturbances may also arise in the head station at Claude Bernard's centre. The number of the neurogenous glycosurias and the toxogenous glycosurias belong to this group as well as the increased excretions of sugar in diabetes under the psychical irritation. However, it is unlikely that influences passing to the liver by path *A*, or path *a*, ever develop more than a transitory effect or at any time produce a chronic form of disease like diabetes. There is more to be said against it than for it.

5. In human diabetes, both in slight and severe cases, the anomalies of path *B* are by far the most important, it may be that either the pancreas itself is diseased and functioning badly or that its energies are paralyzed by outside influences (paths *b*, *b*¹, *b*², and their head stations). The effect of the *b* line stimuli is, however, not of marked importance in most cases of human diabetes. More frequently it happens that the chief disturbance is localized in the pancreas itself and that the impulses, passing down the *b* lines, irritate it only occasionally.

These considerations emphasize the view that diabetes is a complicated disease and show how little aid can be rendered to the patient if the attention is focussed upon the glycosuria alone. The condition demands that the functional powers of all the organs of the body be considered. In order to discover in a case of diabetes the extent of the anatomical and physiological disturbances and the effect of distant organs upon the sugar production a knowledge of physiology and pathology is necessary. Each case is a law unto itself, and marked variations from a common type often occur.

However, no matter where the primary disturbance is localized, or whether one or more of the controlling factors are acting abnormally, in diabetes there is always present an enormous irritability of the *sugar-forming apparatus of the liver*; normal impulses are responded to, not with an ordinary output of the required sugar, but with an extraordinary, almost unlimited sugar production. This lack of coördination between the intensity of stimulus and extent of response is the characteristic feature of the disturbances of metabolism in diabetes. Naturally, there are considerable gradations; at one end the hypersensitiveness of the sugar-forming apparatus is only slight, and is only revealed when the overstraining is specially intense; at the other end the hypersensitiveness manifests itself even to the slightest stimuli. In fact, it is the extent of difference between stimulus and response which determines the severity of the diabetic process.

Marked sensibility of the sugar-forming apparatus and increased production, at once incommensurate and objectless, leading to large losses of sugar, become manifest in each stage of diabetes. All the stimuli which experimental investigation has shown to act as irritants to sugar production exert an increased influence in diabetes: such as the instreaming of carbohydrates and the digestive products of proteins into the liver; acceleration of general metabolic processes by excessive and tiring muscular work or acute febrile attacks; psychical and other nervous excitations; injections of adrenalin; thyroid gland feeding, etc. But these factors do not act equally in every case; from what has been said about the manifold varieties of the stimuli, this will be readily understood.

A recognition of the great excitability of the sugar-forming apparatus and of its tendency to excessive sugar production, as the characteristic features of diabetes, facilitates the appreciation of the problems and aims of a rational form of treating the disease. There is urgent need to calm the excessive irritability of the sugar mechanism. Every unnecessary burden must be avoided. If we are able, by a wise choice of food and the exclusion of other irritants, to lower the demands upon the sugar manufactories the sugar production in slight cases will keep within normal limits, almost without exception, and the glycosuria will disappear. The diabetes

is not cured entirely, for if there again is any overworking of the manufacturing centres they will at once, or in a short time, get out of order. However, the new conditions make for healing or for at least a real and long-lasting improvement. Beyond this Nature herself must make the necessary provision. We have to deal with an every-day experience; if the heart is defective and responds to extra work with rapid or irregular contractions, we protect the heart from added burden; we advise an avoidance of overexertion and overemotion, and then by degrees—if the heart through being spared regains its powers—we gradually and carefully increase the demands for work under close supervision. In this way many hearts regain a normal capacity. Similar examples might be brought forward from the conditions of overstimulation and overstrain of the nervous system, gastric and intestinal diseases, renal diseases, and injury or inflammation of the extremities. In these and other diseases it is necessary to rest the damaged organs. In diabetes, however, this is the exception rather than the rule. The development of the diabetic therapy supplies, perhaps, the explanation. But there are other forces at work also. The patient with heart disease or stomach trouble or injuries to the feet, feels at once when he has overworked the organ; every careless action is followed by a resultant warning pain. The diabetic patient, however, does not feel or recognize the result of the overworking of his sugar mechanism. Only intelligent individuals understand that nervous alteration indicates an overplus of sugar in the blood. A continued daily examination of the urine would supply such an indication, but this would not be possible except in sanatoria or hospitals, and then is of value only if the physician takes into consideration the total sum of impulses which govern the sugar formation (namely, quantity and quality of food, extent of bodily and mental work, presence or absence of complications, etc.). With the usual analysis, once every two weeks or two months, a systematic control is practically impossible. Thus it is too often the case that the organs of the diabetic are overstrained and call for a protective therapy without his being aware of the fact. He feels himself perfectly well. This lack of discomfort as a momentary result of excessive overloading is characteristic of diabetes. The danger lies in the future.

As a rule, the patient does not fully avoid the excessive overloading; there follows a marked irritation of the sugar mechanism; the urine may even still not show sugar to an ordinary analysis, but every such transitory stimulation increases the sensibility of the organs in the future. The more frequently this overloading be repeated the greater will be the difference between the strength of stimuli and the amount of response. Bread and other meal foods which were taken well at first later lead to glycosuria, or, in other words, a slight diabetes shows definite progression. In

addition other disturbances arise, chief of all the formation of acetone and associated substances. This relates to anomalies of the metabolism of fat. Normally, the fat of the tissues is burned to carbon dioxide and water. If, however, during an excessive production of sugar each atom of carbohydrate is removed from the liver as rapidly as it is formed, then the chemical process connected with the cleavage of the fat molecule assumes another type, and acetone bodies result. When large quantities of these are formed there is produced a new danger for the tissues. The presence of carbohydrates (particularly glycogen) is necessary for the cleavage of fat to follow its proper course. It is evident, therefore, that increase of carbohydrates in the food will deal with acetone formation by providing the necessary amount of protective carbohydrates. The worst cases excluded, this certainly leads to the desired end; but it has proved a dangerous type of therapy. The additional carbohydrates constitute an exceedingly strong excitator of the sugar mechanism and damage its regulation more and more. The way to combat the process is to protect the sugar mechanism by sparing its work—by systematic diminution of the carbohydrates as well as of the irritating protein material. Then the excited sugar formation and the acetone bodies decrease. I shall not now enter into the complicated question of the relation of acetone formation to the type of dietary, contenting myself with the remark that this question has assumed too great an importance in the eyes of those in daily practice. To a certain degree acetone formation in diabetes is not at all dangerous. When treated properly it is easier to deal with the acetonuria than is generally supposed.

Since the altered relations between the intensity of the stimulus and the extent of the response show considerable gradations, we may assume that the means of treatment will also call for manifold variation. As a matter of fact, practically all the therapeutic methods find an application in diabetes. Far beyond all others, however, is the treatment by suitable dieting, because food is a factor which acts as a continuous daily renewed irritant of the sugar mechanism, now damaging it or conserving it according to its quantity or quality. The chief excitator among the foodstuffs is the carbohydrate, and its restriction, for more than a hundred years, after many aberrations, has always constituted the most prominent factor of diabetic therapy. The way in which this was done was made a hard and fast rule, and even today, I regret to say, for the most part the same holds true. The worst of these hard and fast rules is that every diabetic is subjected to practically the same restriction of the carbohydrates. The 60 to 80 grams of carbohydrates, which is the amount generally allowed, must in reality, be considered as 80 to 100 grams or more, since the instructions given to the diabetic are, as a rule, not sufficiently precise, and

errors are therefore unavoidable. For a certain number of diabetics 80 + 100 grams of carbohydrates per day is the proper amount, that is to say, the quantity with which the urine remains free from sugar. For the greater number of patients, however, this quantity is not suitable. It may be too high or much too high; or it may be too low or much too low. In both instances the result will be a damage to the tissues. If more carbohydrates are consumed than the liver can utilize in an ordinary fashion, the diabetic disturbances of metabolism increase more and more; in one case slowly, in another rapidly, but in all there is a persistent increase.

After the carbohydrates, there are the proteins to consider as irritants of the sugar mechanism. They pass direct to the liver and there undergo a further cleavage. By this means substances are produced which are transformed easily into sugar. The proteins are, therefore, to be regarded as sources of sugar, although the yield is not great; in fact, it is probably much less than the physiologist assumes. On the other hand, however, the proteins are powerful excitants of the liver cells, and are able to induce marked activity of the sugar-producing centres; in the healthy individual, whose sugar production is strictly controlled by the regulating organs, this excess of activity does not result. In diabetics, however, in whom the regulating apparatus is abnormal the response to these excitants is considerable. The effect of the proteins is not so much that of a source of sugar as it is that of a bellows upon a fire. It incites the sugar manufactories to an incommensurate and unbridled production. The various types of proteins exhibit this character in different degrees, while the hypersensibility of the diabetics to the irritant action of proteins in different cases also shows considerable variation.

The third important foodstuff—fat—does not exert any direct irritant action upon the sugar production. Fat, of course, is a source of sugar, but it plays a passive part, and is thus not comparable with the active powers of the carbohydrates and proteins; it is only used by the liver cells when other material is not at hand. Under conditions of marked excitation of the sugar mechanism, large quantities of fat are utilized and sacrificed. This explains the emaciation which comes on in severe cases of diabetes.

Alcohol is another material which acts as a food and does not irritate the sugar-forming process. On the contrary, it appears to diminish the formation of sugar.

The relations of the several fundamental foodstuffs to the sugar-forming processes in diabetes is thus apparently clear, but the problems of proper dietary are not yet fully solved.

In the foodstuffs used in the natural form or when cooked the fundamental nutrients are mixed in various amounts, and there are in addition other substances, such as alkaloids, acids, ethereal oils, etc. Apparently these compounds exercise an important

action upon the energy of the sugar-forming processes, so that it may happen that two foods which contain an equal amount of starch, and whose protein content does not vary materially, produce different effects when taken by diabetics. Investigations upon this question have not yet advanced to any great extent, but the fact is well recognized and possesses great interest from the standpoint of the nutrition of the diabetic; for instance, in oats there is apparently a substance which acts in such a way as to make oatmeal a better food for the diabetic than some other substances. Of course, certain precautions are necessary. Great heat destroys this substance, and its powers are not very apparent when oatmeal is taken at the same time as other meals or sugars or when the dietary includes meat proteins. Upon this discovery, made ten years ago, I based the so-called "oat cure" for diabetics, and, although the treatment is not applicable to all cases, many have derived benefit from it.

However, all the theoretical knowledge so far gained as to the influence of certain foodstuffs upon the sugar-forming processes does not permit the physician to cease his search for the correct dietary for each single case. It is invariably found that the general rules have to be modified to meet the individuality of the patient. The inexperienced physician only dares to prescribe average dietetic measures. The experienced doctor knows how easy it is by such means for damage to take place, and how important it is that the response of each diabetic to the quantity and quality of the food and to other factors should be ascertained before a plan of treatment is determined upon. This method, first instituted by the late E. Külz, and further expanded by B. Naunyn, I have worked out upon well-adapted lines and am able to recommend its wider acceptance. It is now recognized as the only correct dietetic method of treatment. How different this is from the methods of dietetics in this disease which prevailed in early days! Of 100 cases treated by the newer methods, scarcely 2 receive the same instructions, so various are the graduations and circumstances of each example of the disease.

For each patient there is only one correct method of treatment, and this must be sought for and found. A prolonged experience may make the search more easy, but the desired result cannot be obtained without systematic investigation and observation. For this purpose I generally take the patients into a sanatorium; it is important that the observations should be as exact as possible, for on the results depend the fundamental rules of proper living in the future. In no other way is it possible to avoid errors.

These investigations and a certain form of education or training of the patient are particularly important in the early stages of diabetes. It is a fatal error to assume that slight or occasional glycosurias may be neglected and that they do not call for means of defence.

This assumption is at the bottom of the meaning that diabetes is considered as an incurable disease which cannot be checked. This is not correct. Of course, there are cases of diabetes whose course cannot be checked by any kind of treatment; they are closely connected with a progressive change in the pancreas. Such examples occur chiefly in childhood; in the later decades of life they become more rare. Those cases that are originally simple and slight in type are rather frequent with elderly people. There is no question that the slight type of case may be kept harmless by the employment of a proper treatment. It is necessary, however, that every possible care be taken that the patient adopt a diet which permits him to keep free from glycosuria. This can nearly always be done. The extent of the restriction in food and drink that it is necessary to prescribe, as previously stated, varies considerably with each case. It is as important not to exaggerate the restriction as to be too yielding in the other direction. Should the case at once be led into the correct dietetic equilibrium, then the amount of the restriction and renunciation is not great. It is rather small compared with the advantage we gain and with the dangers we avoid. The loss of the sugar is only the least of the dangers. The chief one in such cases is the excess of sugar in the blood (hyperglycemia). This is always close at hand, even when the urine contains but traces. So long as there is too much sugar in the blood the tissues are subjected to a toxic action and evince a tendency to early malnutrition and disease. Other well-recognized and feared complications of diabetes, as arteriosclerosis, granular kidney, blindness, sciatica and other neuralgias, gangrene, etc., may be attributed to the same cause. They are the most frequent in those cases where slight glycosuria has been present for some years without being controlled. They could easily have been avoided in slight cases if the necessary care had been taken to regulate the intake of sugar-forming materials.

It is for the best interest of the diabetic to observe a strict regulation of the diet, and for a long time he must be careful what he eats and drinks. It would be much more convenient if there were drugs available which would act directly on the sugar mechanism or indirectly through the controlling organs (see diagram) and produce the effect which is attained by dietetic restrictions—namely, a calming of the useless activity of the sugar manufactories. The science of pharmacology teaches that the majority of drugs either excite or depress certain cell groups, such as glandular cells, nerve cells, muscle cells, etc. In the treatment of diseases of the heart, nervous system, digestive organs, etc., drugs prove to be of great value. But pharmacology has not provided any drug which acts directly upon the excitability of the sugar-forming process of the liver. To a certain degree opium is able to exert an influence in this way, but the administration of opium is associated with

so many drawbacks that its employment is much restricted. It is to be hoped that some harmless medicament may be found which will simplify the present dietetic treatment of diabetes. Its lack is the more regrettable, since in consequence of the poverty of scientifically recognized active drugs, many secret remedies and specialities are proclaimed as being specific in action and draw the overtrusting diabetic into their net. It is of interest to examine the grounds upon which the advocates of these remedies base their statements. The manufacturers and salesmen make it clear, either in print or verbally, that while the medicine is being taken the diet must be restricted and contain little or no carbohydrates. As a result the urinary sugar, of course, sinks at once; the chief factor, however, is the well-known dietetic regulation, while the lauded medicine plays only a subsidiary part, and serves—so to speak—as an advertising placard only. Later, the quantity of carbohydrates permitted is slightly increased, just as in scientific medical work, for the directions issued by the manufacturers are copied chiefly from medical handbooks. Perhaps they believe in the efficiency of their remedy rather than in the accompanying dietary. This, of course, is a mistake. There are some, nevertheless, who aim at misleading the public. It is evident that such treatment does not allow of a systematic application of the necessary dietetic restrictions; for this the manufacturer and his medical knowledge do not suffice. One does not find trained medical men giving their advice to such speculators. It is remarkable that some physicians fall a prey to the claims of these secret remedies; it is to be supposed that they do not understand the principles underlying the dietetic treatment of diabetes. It may be they learn that one of their patients is undergoing one of these cures; the prescribed diet happens to be the correct one for the patient, and the result fills the doctor with astonishment. The lack of his judgment and criticism lead him to accept the belief that something has happened which the scientific physician could not accomplish. He is only right, however, in that he personally is unable to induce the result; and he is wrong and even blameworthy if he identifies his own capabilities with medical science. The only apology for his standpoint is that dietetic therapy in general and that of diabetes in particular demands a considerable amount of special knowledge, and that clinical instruction in this important matter was in the early days extremely poor, while there are even now many clinics in which there is much to be desired in this regard. The activity of the manufacturer and vendor of these specialities, and, on the other hand, the surrender of the patients to the mercy of these wonder cures, are to be regretted, because attention is diverted from the most important therapeutic factor (dietetic observances), or the restriction of the diet is simply on the lines

of hard and fast rules and not suited to the special requirements of each individual case. The dangers of the condition persist even if the pretended medicament consists only of harmless vegetable extracts.

It may occasion some wonder that mineral water cures are not here mentioned as a method of inducing a restriction of the sugar production. They stand in high esteem, and the great majority of patients place upon them much higher worth than that of regulating the diet. Karlsbad, Neuenahr, and Vichy are the chief favorites. The fame of these places could not be maintained if the patients did not derive some benefit from them. It is well known that the waters do not exert any demonstrable influence upon the production or excretion of sugar or upon the intensity of the diabetic processes. The value of a residence in these resorts lies in the fact that at least for a month the patients live, eat, and drink in a rational manner. In addition, the absence of the worry and irritation of every-day life tend to diminish the general nervous tension and to weaken the force of any irritating stimuli proceeding from the central nervous system to the organs concerned in the sugar mechanism. In the mild cases of diabetes there is also the favorable influence of the regular exercise, which is enjoined here, upon the glycosuria; in the severe cases the opposite effect may result. Many diabetics exhibit also certain complicating disturbances of the stomach, intestine, liver, kidney, etc., and upon these the mineral waters undoubtedly act in a favorable manner, and thus play a part in bringing about an increase in the general well-being.

If, on the other hand, the value and influence of the mineral-water cure be exaggerated, there is constituted a certain danger for the diabetic in that he believes he has done all that is necessary to maintain his health, and that he is not required to insure a proper living and proper eating by putting a curb upon his wishes. Hence, the fate of his life depends, and this is essential, not upon a month's treatment at a watering place, but upon the systematic continuance of a proper regime for the remaining eleven months of the year. It is for the best interests of the diabetic that if he wishes to maintain his health he must guard himself against an overindulgence in food that is detrimental to his well-being, even when he feels in fairly good health. He has to deny himself for the present in order that he may reap in the future. We cannot obviate this necessity in any way. The patient learns it if he is rightly instructed; and that what at first is only attained by struggle and self-denial, later on becomes second nature. The doctor who is responsible for the health and life of the patient has to fix his mind upon what the future shall bring. He must not allow himself to be influenced by the transitory likes and dislikes of the patient, but must prepare for later developments. In preparing his scheme

of treatment for this year the physician must have in view what will be the effects on the diabetic patient many years hence. If both doctor and patient keep their eyes fixed on this object, the necessary amount of restriction will appear not as a burden, but as a welcome benefit.

EXTRACARDIAC CAUSES OF FAILURE OF COMPENSATION IN VALVULAR DISEASES OF THE HEART.

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THE point of view of clinicians regarding cardiac pathology has always been too narrow, because they have appealed to the pathological anatomist for their data and have ignored the teachings of physiology. The solution of many questions in the pathology of the circulation lies entirely outside the domain of mere morphology and for this reason certain prevailing views of disturbances of the circulation and methods of treatment based upon such views, sadly need revision. It is a well-known fact that in cases of death following valvular disease of the heart the pathologist finds in the heart only the valvular defect and certain alterations in the myocardium and outside the heart only peripheral and visceral lesions that have resulted from passive congestion. There is nothing to indicate clearly the steps that have led from the original valvular defect to the final cardiac breakdown, nor can we hope for a solution of this important chain of events from morphological studies made after death. The intermediate stages between the valvular disease and the hopelessly dilated heart are unexplained, and seem, therefore, because so frequent, the inevitable tendency of a progressive disease. The nomenclature we use itself establishes wrong impressions leading to the same assumption of inevitable cardiac breakdown. We speak of "chronic" endocarditis, but this is a misnomer. Strictly speaking, chronic endocarditis is not a chronic disease at all in the sense that it represents a chronic and continuing process. Rather it is a result of previous acute or subacute disease, and ceases to be progressive when the damage has been done. There are undoubtedly some exceptions to this rule, as in the case of certain types of infective endocarditis and syphilitic disease of the heart; but for the most part what we recognize as chronic endocarditis or valvular disease is a deformity that has resulted from a past affection no longer active or progressive. The same thoughts apply in a lesser degree to chronic myocardial disease, though here it is probable that the process more frequently

is truly a chronic and continuous one. It is important to note that compensation is established *after* the valvular defect has been completed, and that the compensating heart is capable of maintaining its share in the work of the circulation, with some reserve power to spare, though less than the normal heart possesses. If then a lesion of a valve no longer active or progressive has been followed by satisfactory compensation with some reserve power, why does the heart fail and often before the involutional processes of age might be presumed to have weakened all organs including the heart? The clinician leaning upon the pathological anatomist, who has invariably found a degenerated and dilated heart, has concluded that this is the inevitable outcome, and misled by the inference implied in the name has accepted the result as the necessary consequence of a chronic disease. Romberg (*Krankheiten des Herzens*, second edition, p. 72) very properly states that "Hypertrophy as such does not carry with it the germs of later cardiac weakness through gradual exhaustion or the like."

The fault of the pathological anatomist and clinician alike has been that they have kept the heart itself too conspicuously before their attention, and have failed to realize that other factors outside the heart are of almost equal importance in maintaining the circulation. Placed at its centre the heart is undoubtedly the chief factor in the circulation, but without the coöperation of other agencies, mainly concerned with the regulation of peripheral circulation and with the return of the blood to the heart, cardiac power, however great, must prove unavailing. The work of the heart is expended in propelling the blood through the arterial system and arterioles into the capillary bed or through it to the veins. Here stagnation must occur if other factors did not avail to carry the stream onward through the veins. Excess of cardiac power would not be effective to drive the blood through the capillaries and into the veins under sufficient pressure to insure a return flow to the heart, for the reason that the vasomotor mechanism by contracting the arterioles interposes a resistance, and thus incidentally saves the capillaries from the injurious pressure that would break their delicate walls. The return circulation is almost wholly due to agencies outside the heart, and it is to these that the clinician must give his thought when the causes of failure of cardiac compensation are under consideration.

While it is my purpose here to emphasize the important bearing of conditions outside the heart in the eventual occurrence of failure of compensation (and if I give undue emphasis it is because this field has been neglected), it would be unfair to ignore the fact that clinicians and pathological anatomists have made clear certain conditions under which a heart the seat of valvular disease may become additionally damaged so as to become insufficient. For example, it is well known that various infections or undue physical

strains may be the occasion of rapid failure of such a heart, and long-continued strains, not immediately injurious, may gradually break down the reserve power of a heart already crippled by a valvular defect. But instead of searching industriously in all cases for some such explanation of the cardiac failure, one should review all of the factors concerned in the circulation outside as well as in the heart itself to determine if possible the cause of the overstrain. A survey of the chief agencies which participate in the circulation with some illustrations of the way in which their inadequacy may operate will serve to make clear some of the problems in the study of cardiac decompensation.

The Circulation in the Arteries. The all-important factor in maintaining a sufficient blood pressure in the arterial system and in driving the blood toward the periphery is the contraction of the left ventricle. Aided by the valve mechanisms of the heart this force drives the blood into the aorta and other large arteries under a relatively high pressure, which causes these vessels to distend. At the onset of ventricular diastole the aortic valves close and the elastic recoil of the large vessels drives the blood onward toward the arterioles and capillaries. No other propelling force operates in this field, and the maintenance of the arterial circulation, therefore, depends upon the driving power of the heart and the condition of the arterial system and the blood. In the arteries elasticity, the condition of their lining membrane, and their caliber are of importance, and the activity of the vasomotor mechanism is of particular consequence. The condition of the blood as to viscosity or bulk may be a far more potent item than we ordinarily allow. Failure of the cardiac power, and, therefore, failure of the arterial circulation, may be the direct result of progressive or intercurrent cardiac degeneration, with dilatation. Thus in cases of coronary sclerosis and thrombosis there may be a rapid failure of the ventricle, or acute myocardial disease following some infection may be the occasion of cardiac breakdown. But in the majority of cases of cardiac disease such factors are not discoverable. The explanation may in some be found in other conditions on the arterial side of the circulation. For example, a constantly recurring cause in clinical experience is arteriosclerosis. A person suffering from some cardiac disease may maintain adequate compensation until after middle life arteriosclerosis supervenes. The increased stress laid upon the heart by the inelastic vessels then occasions gradual failure until eventually the ventricle dilates and becomes wholly insufficient. Similarly, certain vasomotor conditions operating mainly upon the arterioles may be the occasion of the cardiac overstrain. Thus in renal disease the constant hypertension of the arterial system tends to exhaust a normal heart and even more speedily one already crippled by valvular disease. The bearing of the vasomotor mechanism and of conditions of the blood on

cardiac decompensation will be referred to later in somewhat greater detail.

The Circulation in the Arterioles and Capillaries. The chief factor in maintaining the flow of blood through the arterioles and capillaries is still the force of the ventricle. In the case of the capillaries certain subsidiary agencies, such as the elastic condition of surrounding tissues, the contractility of the capsules of certain organs, and muscular contractions are to be remembered; but the *vis a tergo* is doubtless chiefly responsible for the onward movement of the blood. The arterioles hold to the capillaries the relation of a buffer, which serves to protect these thin-walled vessels from the destructive pressure of the arterial system, and they at the same time operate in a protective way toward the heart through the activity of the vasomotor mechanism when undue strains threaten sudden cardiac dilatation. Their protective office toward the heart is well illustrated in aortic regurgitation, in which their dilatation reduces peripheral resistance to a minimum and relieves the heart of injurious back pressure. Studies of blood pressure in various parts of the circulation show a rapid diminution from the arteries to the capillaries. Taking as approximate estimations a pressure of 150 mm. in the aorta and the large arteries and but little less in the small peripheral arteries, 20 mm. in the capillaries, and 6 to 7 mm. in the peripheral veins, this rapid diminution in the arterioles will be evident. Formerly it was thought that much of the blood pressure was expended in overcoming resistance in the capillaries, but such figures as the above, which are approximately trustworthy, will show the contrary, as but one-tenth of the blood pressure was utilized in the capillary area. B. Lewy¹ has made calculations which seem to show that but one-fourteenth of the blood pressure is consumed in the capillaries, from which it is apparent that the chief resistance to the blood flow is in the arterioles. Campbell has pointed out that if the capillaries introduced a very considerable degree of resistance so that the pressure at the beginning would necessarily be higher than at the end their thin walls would make a funnel shape a necessary result, which is not the case.

The vasomotor mechanism is mainly operative upon the arterioles and through the contraction or dilation of these vessels regulates blood pressure as a whole and the distribution of the blood in different organs. The integrity of the whole mechanism is dependent not only upon the normality of the arterioles and the nerve centres and fibers that make up the vasomotor system, but also, and perhaps in specially important ways, upon various internal secretions or products of tissue metabolism. Organic change in the arterioles is probably always associated with change in the larger arteries

¹ Quoted by Tigerstedt.

and the influence of such changes on the work and eventually on the preservation of the heart is commonly recognized. Changes in the nervous mechanism are little known except such as accompany certain organic diseases of the central nervous system and acute infections, as well as certain so-called neuroses. A much larger group of conditions as yet but imperfectly known is that in which the internal secretions or metabolic processes suffer derangement to the detriment of normal vasomotor conditions. The high pressure of nephritis and the low pressure of Addison's disease may be cited as extremes, but there is probably a large number of less conspicuously active conditions in which vasomotor disturbances play an important role. It is impossible at the present time to specify the directions in which various nutritional disorders operate, but it is safe to assert as a generalization that a number of diseases or conditions attended with nutritional or metabolic disorders act injuriously upon the vasomotor system and eventually serve to overtax cardiac power. We may therefore in many cases seek in this direction for an explanation of the final overthrow of a heart in which valvular disease has existed.

The splanchnic circulation is of special interest in connection with the whole vasomotor mechanism, as it is by far the largest vascular field in the body and the one most immediately involved in vasomotor influences. Closely connected with its peculiar responsiveness to vasomotor control is its constantly recurring activity in the processes of digestion. One need but recall the enormous repletion of the mesenteric and intestinal vessels in an animal killed while the intestinal canal is overfull and the relatively ischemic conditions in the fasting animal to gain an impression of the possible bearings of habitual overfeeding as contrasted with moderation. Recent investigators have sufficiently proved the influence of sclerosis of the mesenteric vessels in determining systemic hypertension, but doubtless long before such organic changes have taken place in the bloodvessels, recurring or continuous taxations upon the splanchnic mechanism may influence injuriously the circulation as a whole. Not only conditions of hypertension but repletion of the abdominal circulation may act injuriously, as is shown by the fact that rabbits may be killed by holding them upright and thus causing overfilling of the vessels of the splanchnic area.

Clinical experience abundantly confirms the results of experimental investigation in showing how greatly continued overdistention of the splanchnic circulation taxes the whole circulation and eventually the heart. One of the commonest types of anginoid conditions of the heart is that which occurs in overfed men with large and perhaps somewhat pendulous abdomens. In such individuals, circulatory disorders are often encountered after middle life when previously every indication of robust health had existed.

After the age of fifty to fifty-five years, evidences of cardiac weakness may make their appearance—impure heart sounds, a systolic mitral murmur, signs of dilatation, undue dyspnea on slight exertion, mild anginal pains, and eventually cardiac failure. The explanation of these symptoms may be found in myocardial disease which has resulted from long-continued overfeeding and disturbance of normal metabolism, but probably in a more direct way impediments in the splanchnic circulation have affected injuriously the general circulation and the cardiac power. The beneficial effect of abdominal support and of careful regulation in diet in such cases is a suggestive evidence that the difficulty is more largely a matter involving the mechanical conditions of the abdominal circulation and perhaps its vasomotor mechanism than one occasioned by preëxisting myocardial disease. Finally, however, if conditions are not improved actual dilatation of the cardiac chambers results, and it is not often easy to determine whether a toxic weakening of the heart muscle or some extracardiac disturbance of the circulation has been mainly at fault.

The Venous Circulation. On the venous side of the circulation the important factors are: (1) Muscular contractions, (2) the valves in the veins, (3) the normal tissue tone, (4) the aspirating effect of the movements of the chest, and (5) gravity.

Muscular contractions are of prime importance in forcing the blood through the veins toward the heart. The value of this factor in the circulation is evident when one recalls the increased flow of blood from a severed vein of the arm upon voluntary contractions of the muscles of the forearm and hand in opening and clenching the fist. Less demonstrably but none the less certainly the effect of athletic exercise upon the circulation illustrates the influence of muscular contractions in furthering peripheral circulation. On the contrary, one sees in those who are habitually sedentary the evil effects resulting from a lack of muscular contractions, and especially in those whose occupations requires much standing without muscular exertions to change position or in convalescents whose weakness prohibits active use of the lower extremities. In these conditions (in which doubtless vasomotor conditions also play a part) there is a tendency to venous stasis which gradually operates in the direction of overtaxing the heart, partly by introducing an obstruction in front of the arterial circulation and partly by depriving the heart of an adequate return flow.

Another effect of muscular exertion is quite apart from the direct effort in compressing the veins and forcing the blood toward the heart. This is the suction action which the stretching and increase of capacity of the veins occasion when certain sorts of muscular effort are employed. When the arms are widely extended and the body is thrown back there is an appreciable increase in the capacity of the large veins and a tendency to draw the blood

toward the heart. This explains to some extent at least the desire of persons who have been for some time in a cramped position to stand and extend the arms.

The effect of the venous stasis that results from lack of muscular contractions in such conditions as sedentary life, standing occupations, prolonged weakness after illness, and paralysis of the extremities is at first confined to the venous side of the circulation and is manifested by coldness, lividity, and edema of the extremities. Eventually, however, if such venous stasis is extensive the heart itself and the arterial side of the circulation must suffer because, as before stated, an adequate return supply of blood to the heart is wanting and on the other hand the resistance in front of the capillaries to some extent retards the arterial flow. Such impediments to the peripheral circulation unless very extensive can have little effect upon a normal heart, but can more readily injure one that is already weakened by a valvular lesion.

The effect of deficiency in the muscular contractions—thoracic, diaphragmatic, and abdominal—concerned in respiration has a somewhat different explanation from that applying to the peripheral muscular system and will, therefore, be considered separately.

The valves of the veins are an important adjuvant to muscular action in directing the return circulation of the blood. One sees the immediate results of their insufficiency in the extreme venous repletion that occurs in cases of phlebectasis. Thus in women who have extensive varicosity of the veins of the legs after repeated childbirths a large part of the blood of the body may be stagnated in the lower extremities and cardiac weakness, palpitations, faintness, vertigo, and other symptoms of circulatory derangement may result. These symptoms may be controlled by narrowing the venous bed by the application of elastic bandages.

Tissue tone is an indefinite, though doubtless real, condition which may be of considerable importance in regulating peripheral circulation. Its absence is more demonstrable than its presence, as, for example, when the relaxed conditions of paralysis or following protracted illness determine stasis of the peripheral circulation and edema. Compared, however, with muscular activity this factor is of little importance in the return circulation, and its absence plays no conspicuous part in determining circulatory derangements.

The aspirating effect of movements of the thorax in respiration is a factor of prime importance in the venous circulation. During ordinary respiration the pressure in the large intrathoracic veins is approximately 6 mm. of mercury; during forced inspiration it may be depressed to 20 mm. The effect of such reduction of the central venous pressure must be obvious. On the contrary, conditions such as emphysema of the lungs, intrathoracic effusions, tumors, etc., in which thoracic expansion is interfered with, occa-

sion marked peripheral congestion by reducing the aspiratory influence of free movements of the chest.

The act of respiration is also of assistance in the return circulation of the blood in another way. The contractions of the abdominal muscles and of the diaphragm by compressing the abdominal viscera tend to expel the blood from the abdominal circulation and force it toward the heart.

Clinical observation abundantly illustrates the beneficial effects of respiration in maintaining proper circulation, and even more clearly demonstrates the unfavorable effects of conditions in which the respiratory movements are deficient. Not only does one see this in the well-known effects of emphysema of the lungs, pleural effusions, tumors, aneurysms, and other intrathoracic diseases, but also in the circulatory weakness that results from abdominal obesity, enteroptosis, and other abdominal conditions which interfere with the normal activity of the diaphragm and abdominal muscles. Abdominal fatness in particular is of clinical importance, and seems after middle life to be the frequent cause of failing cardiac power. In such cases one must recognize several operative factors, such as the influence of disturbed vasomotor conditions, of gravity, and perhaps of associated fatty deposition in and about the heart; but in addition to these, the effect of decreased respiratory activity must be considered. A significant proof of this is manifest in the improvement obtained in such cases by systematic respiratory exercises.

Gravity is an aid to the circulation only in the case of that of the head, where, it may be observed, muscular contractions play less of a part in assisting the return circulation than in the extremities and trunk. It is a force that needs to be overcome by other factors in the abdomen and limbs, and under certain circumstances becomes a considerable obstacle to the return flow of blood. Thus in occupations requiring prolonged standing there is a pronounced tendency to stasis in the legs, and doubtless in elderly individuals with pendulous abdomens the same influence affects the abdominal circulation injuriously as it does in animals held in an upright position. In persons convalescent from acute diseases one frequently finds that this cause together with vasomotor weakness, muscular atony, and loss of tissue tone determine the occurrence of edema of the feet. Eventually such peripheral stagnation has an unfavorable effect upon the heart and the arterial side of the circulation.

The Effect of Quality and Mass of Blood on the Circulation. The viscosity of the blood is manifestly of importance in the determination of the work of the heart, but we lack precise data to estimate this factor properly. Such facts as are available indicate that excessive eating and especially excessive meat eating, as well as faulty renal elimination, tend to increase the viscosity of the

blood and thereby increase the work of the heart. How much the condition is responsible for the circulatory difficulties of overfed and overfat individuals as contrasted with the effects of impaired muscular activity, of reduced respiratory activity and of gravity must be a matter of some uncertainty. The rather immediate effect of overfeeding, without injurious overdistention of the stomach, that is observable in some cases of cardiac weakness would suggest that the conditions of the blood resulting therefrom may be of material consequence. A medical man, himself a considerable student of cardiovascular troubles, informs me that he has invariably suffered attacks of acute pulmonary edema and cardiac asthma after meals rich in protein, and that by care to avoid such a dietary he has been able to avoid their occurrence. This may of course be explained on other grounds, but is at least suggestive in the direction of possible modification of viscosity of the blood.

Increased quantity of blood or plethora vera is a condition which clinical observation as well as experimental investigation have shown to be at the most of brief duration. The introduction of excessive amounts of fluid either through the gastro-intestinal tract or into the veins is speedily followed by vasodilatation, exudation, and glandular activity which restore the normal pressure of the vascular system. Though a permanent plethora vera does not occur, a temporary overfilling of vessels may result from excessive ingestion of fluid, and clinically, as well as experimentally, dilatation of the heart has been observed, and some cases of sudden death have probably resulted from this condition. Often no doubt persons affected with some form of cardiac weakness suffer from repeated strains due to temporary overfilling of the vessels as a result of excessive drinking of water or other liquids. Oertel long ago pointed out the unfavorable result of a too liberal ingestion of fluids by persons suffering from cardiac weakness, and an abundance of clinical observation confirms his views in this particular.

The Conservative Relations of the Liver and Spleen to the General Circulation. The capacity of the liver and spleen for blood is considerable and clinical, as well as experimental, evidence in abundance shows that these organs are capable of enormous vascular distention at times when the overfilling of the vascular system threatens cardiac dilatation. Experiments to determine the degree of acute plethora that may be sustained without injurious consequence by intravenous injection of salt solution show that the liver undergoes enormous enlargement before any signs of dilatation of the heart become manifest. Clinically it is well known that the liver enlarges and contracts in cases of cardiac disease in proportion as cardiac compensation is maintained or deficient, while the general circulation shows no commensurate

fluctuation in venous repletion. The conclusion from such observations must be that the liver acts in a measure as a safety reservoir to protect the right heart against overfilling.

The spleen as a subsidiary of the portal circulation aids in the same direction. In the later stages of chronic cardiac disease when secondary induration of the liver has occurred, and distention becomes difficult or impossible, the protective influence of the liver is lost and cardiac dilatation soon occurs.

Having reviewed in this rather brief and undetailed manner a variety of extracardiac adjuvants of the circulation, it is proper to conclude that there are many directions in which one must seek for the occasion of cardiac overstrain when a heart previously damaged by endocardial disease begins to fail in its compensation. The tendency to which I alluded in the beginning of my remarks, and which is largely attributable to the dominating influence of pathological anatomy in our clinical deductions, has been to regard the heart as somehow foredoomed to failure in such cases. My own clinical experience, however, in conjunction with a consideration of the physiological data I have here sketched in outline have led me to believe that the causes of final cardiac failure are usually quite outside the heart itself. Lack of regulated exercise, habits of overeating, obesity, disturbances of the abdominal circulation, improper breathing or thoracic diseases, and conditions of the blood are among these extracardiac conditions that may be of importance. I have alluded to the possibility that metabolic disorders may play some part by exercising an unfavorable influence on the vasomotor system or on the viscosity of the blood, but do not dwell upon these because the data are not sufficient to justify more than a hint at the importance of such conditions. It would have been proper to enlarge upon the effect of advancing arteriosclerosis and its attendant hypertension in determining cardiac breakdown in cases of old valvular disease, but this is a fact so well recognized that I have ignored it in order to keep other and less frequently considered conditions more prominently in mind.

What I have been attempting to bring forward must not be thought to have merely an academic interest. It is an intensely practical matter for the physician who has to deal with cardiac disease from the time of its inception to the final termination. He has been properly advised to avoid medication during the stage of compensation, and has in a general way been instructed to pay particular attention to the hygienic regulation of the patient's life; but he has had little guidance regarding exact details based upon a recognition of the probable causes of subsequent cardiac failure. Physician and layman alike have been aware that physical or nervous strains, exhausting occupations, lack of proper sleep, and similar conditions are injurious because they tend to exhaust

cardiac power, and the pathologist has shown how intercurrent infectious diseases may operate unfavorably by causing myocardial complications, but aside from such knowledge, there has been little to guide the practitioner in the management of compensated cases of cardiac disease. The too one-sided view of the problem and one concerned only with upholding the myocardial efficiency has indeed led to certain decidedly disadvantageous methods of treatment. For example, the desire to avoid physical strain has occasioned a common practice of denying all exercise to persons with compensated lesions. In view of what has been before stated, this tends to retard the proper return circulation and to bring about all the unfavorable effects of sedentary life. Moderate and well-regulated exercise is, on the contrary, of the greatest advantage during the stage of compensation, and even after the reserve power is beginning to be deficient. In the matter of diet, also, the over-emphasis placed upon the integrity of the heart muscle has sometimes occasioned erroneous practice. In the effort to keep the heart well nourished and perhaps establish better compensation, a liberal and often excessive dietary has been advised, and doubtless unfavorable results have often resulted. Finally, when compensation has begun to fail, the monopoly of responsibility has been laid upon the heart itself, and no other course suggested than to resort to stimulants or general and cardiac tonics. Fortunately there has been some improvement in the management of circulatory disorders in recent years, thanks to the labors of those who have busied themselves with mechanical, physical, and hydrotherapeutic measures; but the possible usefulness of these agencies has been so generally associated in the mind of physicians with certain health resorts that far too little effort has been made at home treatment along the same lines. In the last analysis it will be found that even at this day practically all cases of beginning cardiac decompensation are relegated to purely medicinal treatment. Not even the excellent scientific investigations of the last decade with new and refined instrumental methods of study have availed to correct matters, for here again the heart itself has been mainly the object of study, and but little attention has been given to the practical bearings of the peripheral circulation. I have not had the purpose, even remotely in mind, to undervalue the importance of the heart itself, but rather to point out that the circulation must not be looked upon as a system of tubes through which the blood is bound to flow smoothly so long as the central driving force remains intact. Nothing could be farther from the truth. If it were true we would be justified in bending every effort to the maintenance of the cardiac power without regard to the rest of the circulation. As it is not so, the physician will do well to consult the physiologist to learn in what manner the whole circulatory system is regulated, and how it compensates for imperfections

in one place or another. The conclusions that necessarily follow such an inquiry are the occasion for the discussion I have presented.

THE KINETIC THEORY OF GRAVES' DISEASE.

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LET us first point out some of the shortcomings of the leading hypotheses held at present—namely, the auto-intoxication, the infections, the nervous, and the thyroid hypotheses. The auto-intoxication and the infection hypotheses do not explain why cretins do not have Graves' disease, and why the disease so frequently follows in the wake of some strong emotional excitation and is engrafted on colloid goitre, benign tumors, and even cancers of the thyroid gland; nor do they explain those cases caused by excessive dosage of thyroid extract or of iodine, nor the relation of Graves' disease to adolescence or to pregnancy. The infection and the auto-intoxication theories are not at present widely held, and their basis seems insecure.

The two hypotheses that have the strongest support at present are the nervous origin and the thyroid origin. The theory that the disease is primarily in the nervous system scarcely explains the cases whose origin lies in excessive doses of thyroid extract, nor the cures wrought by excision of a lobe, or ligation of the poles of the thyroid, nor does it explain the constant presence of hyperplasia of the thyroid.

Those who believe that Graves' disease is a disease of the thyroid gland alone, and may be regarded as a hyperthyroidism, must, on the other hand, be at a loss to explain the frequent cure by physiological rest and the relapses that may occur after an apparently sufficient amount of the gland is removed if the patient is again submerged in the environment that originally produced the disease. If Graves' disease is simply a thyroid problem, then if the operation has removed a sufficient amount of gland there should follow at once a cure just as definite as the symptoms of hyperthyroidism due to overthyroid feeding are relieved on withholding the thyroid extract. This, of course, does not follow. It is difficult to understand how the thyroid hypothesis accounts for the cases induced by nervous strain, and how it accounts for the cases in which the administration of thyroid extract in colloid goitre causes the disease, because usually the effect of thyroid extract and of iodine is to diminish the activity of the thyroid—as seen in the disappearance of goitre in adolescent girls.

These two hypotheses harmonize many of the facts, but apparently neither is adequate; but the true hypothesis must surely account for the lesions of both the nervous system and of the thyroid gland. But in its gross pathology there is practical agreement. Lesions are found in cells of all parts of the cerebrum, the cerebellum, to a less degree of the medulla, and little or not at all in the spinal cord. The heart, voluntary muscles, the thyroid, the adrenals, the pancreas, the liver, the lymphatics, the thymus, the spleen, the lymphatic glands, the skeletal muscles, the skin, the bony skeleton, the teeth, the hair all show pathological modifications of varying degrees according to the duration and the severity of the disease. *Nearly all of these structural changes may be produced by the emotions.* The significance of this will be later seen. From the foregoing it is obvious that whatever the cause it is a malady of protean manifestations.

Diseases are assigned to classes they most resemble. Does exophthalmic goitre closely resemble any disease? I know of none. Does it resemble so closely that it might be related to any normal process? Clinicians have always remarked upon its resemblance to the emotions, especially that of fear and the exhaustion of over-exertion. We will first compare the phenomena of Graves' disease and those of fear and worry.

The following phenomena of worry, nerve strain, and fear are nearly identical with the phenomena of Graves' disease—namely, increased heart beat, increased and altered respiration, rising temperature, sweating, muscular tremors, protruding eyes, loss in weight. Cannon has found an increased amount of adrenalin in the blood in fear; in each there is increased blood pressure; muscular weakness; digestive disturbances; falling out of the hair; decay of the teeth; skin eruptions; disturbance of the growth and change in texture of the nails; impaired nervous control; hyper-susceptibility to stimuli; lack of initiative, and decreased mentality. In protracted intense fear the brain cells show marked physical changes. In Graves' disease analogous changes are seen. Disregarding the thyroid and the exophthalmos, if the symptoms of acute fear continued for weeks and months, who could differentiate between Graves' disease and fear?

Surely the phenomena of Graves' disease and those of the emotions present a striking resemblance even in their minor details. The first question that arises is what is the origin of the emotions? What is the purpose of their phenomena and may Graves' disease and the emotions have a common origin? The former represent a normal process and the latter a pathologic.

It may be assumed that the same principles underlie the emotions of fear and of anger and of sexual love.

I shall limit my discussion mainly to the strongest emotion, *fear*. I believe that it can be shown that the emotion of fear can

be elicited only in animals that utilize a motor mechanism in defence against danger or in escape from it. The defence of the skunk is a diabolic odor which repels its gross enemies. The skunk has no adequate equipment for defence or escape by muscular exertion. The skunk has little or no fear. Certain species of snakes are protected by venom. They possess no other adequate means of defence or escape. They show no fear. Animals having mechanical protection, as the turtle and porcupine, have little fear. Other animals because of their prowess have but few fears. The lion, the grizzly bear, the elephant are examples. It is obvious that fear is not universal. The emotion of fear, as I believe, is felt only in those animals whose self-preservation is dependent upon the uncertain adequacy of their power of muscular exertion, either in defence or in flight.

What are the principal phenomena of fear? They are palpitation of the heart; acceleration of the rate and alteration of the rhythm of the respiration; cold sweat; rise in body temperature; tremor; pallor; erection of the hair; increase of certain internal secretions; suspension of the principal functions of digestion; muscular tremors; protrusion of the eyes; the function of the brain is wholly suspended, except that which relates to the self-protective response to the object feared. Neither the brain nor any other organ of the body can respond to any other lesser stimulus during the dominance of fear.

From the foregoing it would appear that under the influence of fear, most, perhaps all, of the organs of the body are divided sharply into two classes: (1) Those that are stimulated, and (2) those that are inhibited. Those that are stimulated are the entire muscular system; the vasomotor and locomotor systems; the senses of perception; the respiration; the mechanism for erecting the hair; the sweat glands; the thyroid gland; the adrenal gland (Cannon); the special senses. On the other hand, the digestive and procreative functions are inhibited. What is the significance of this grouping? So far as we know the organs stimulated increase the efficiency of the animal for flight or for fight. It is through skeletal muscles that the physical attack or escape is effected; these muscles alone energize the claws, the teeth, the hoofs, and the means for fight or flight. The increased action of the muscles of the heart and the bloodvessels increases the efficiency of the circulation; the secretion of the adrenal gland causes a rise in the blood pressure; the increased action of the thyroid gland causes an increased metabolic activity; there is evidence that glycogen is actively called out, it being the most immediately available substance for the production of energy; the increased activity of the respiration is needed to supply the greater requirements of oxygen and the elimination of the increased amount of waste products; and regulation of heat supplying the increased

activity of the sweat glands is needed to regulate the rising temperature of the body due to the increased metabolism. The activity of all of the organs of perception—sight, hearing, smell—is heightened for the purpose of perceiving the more accurately the danger. It could not be a mere coincidence that the organs and the tissues that are stimulated in the emotion of fear are precisely those that are actually utilized in the perception of danger and in a physical struggle for self-preservation. Among the organs inhibited are those that have mainly to do with digestion and procreation, and the muscles that are not concerned in a physical defence or escape.

Are there any other organs stimulated by fear except those that can or that do assist in making a defensive struggle? I know of none. On the other hand, if an animal could dispense with his bulky digestive and other organs, whose functions are suspended by fear—if he could, so to speak, clear his decks for battle—it would be advantageous. Although the marvelous versatility of natural selection apparently could devise no means of affording this advantage, it did the next best thing—it turned off the nerve current and saved the vital force these non-combatants ordinarily consume in the performance of their functions. Whatever the origin of fear is, its phenomena are due to a stimulation of all of the organs and tissues that add to the efficiency of the physical struggle for self-preservation through the motor mechanism and an inhibition of the functions of the leading organs that do not participate—the non-combatants, so to speak. Fear arose from injury. By the slow process of a vast empiricism nature evolved the wonderful defensive motor mechanism of many animals and of man. Now the stimulation of this mechanism leading to a physical struggle is action; and the stimulation of this mechanism without action is emotion.

We may say then that fear is a *phylogenetic fight or flight*. On this hypothesis all of the organs and parts of the entire animal are integrated, connected up, or correlated, so that the motor mechanism may play its maximum role in self-preservation. Man fears not in his heart alone, not in his brain alone, not in his viscera alone, but he fears in every organ and tissue of his body; each organ or tissue apparently is stimulated or inhibited according to its help or hindrance in the physical struggle for existence. In thus playing all or most of the nerve force on the nerve-muscular mechanism for defence alone a greater physical power is developed, hence, it is that animals or men under the stimulus of fear may be able to perform preternatural feats of strength. Then, too, for the same reason the exhaustion following fear will be the greater, as the powerful stimulus of fear drains the cup of nervous energy, though no visible action may result. An animal under the stimulus of fear may be likened to an auto-

mobile with the clutch thrown out, but whose engine is racing at top speed. The gasoline is being consumed, the complex machinery is being worn out, but the machine as a whole, does not move, though the power of its engine may cause it to tremble. In applying this conception to human beings today it must be borne in mind that man has not been presented with any new organs to meet the requirements of the present state of civilization; indeed, not only does he possess the same type of organs as his savage fellows, but also the same type of organs possessed by the lower animals. In fact, the present work of civilization of man is now operated with the primary equipment of brutish organs. Contrasted with the entire duration of organic evolution, man has come down from his arboreal abode and resumed his new role of increased domination over the physical world but a moment ago. And now sitting at his desk in command of complicated machinery of civilization, when, for example, he fears a business crash, it is in the terms of his ancestral physical battle in the struggle for existence. He cannot fear intellectually, he cannot fear dispassionately; he fears with all his organs, and the same organs are stimulated and the same organs are inhibited as if instead of being a battle of credits, or position, or honor it were a physical battle with teeth and claws. Whether the cause of acute fear is moral, financial, social, or stage fright, the heart beats wildly, the respiration are accelerated, perspiration is increased, and there is pallor, trembling, indigestion, and so forth. The phenomena are those of physical exertions for self-defence or escape. There is not one group of phenomena which expresses the acute fear of the trusted official who suddenly and unexpectedly faces the naked probability of the penitentiary; another for a patient who unexpectedly finds he has a cancer; or for the hunter when he shoots his first big game; or for the passenger in a railway wreck; or the animal in the wilds confronting a formidable enemy. Nature has but one means of response, and whatever the cause, the phenomena are always the same—always physical. All forms of fear as it seems to me express themselves in similar terms of ancestral contests, and on this law dominate the various organs and parts of the body. Anger and fear express opposite states. Fear expresses the evidence of a strong desire to escape from danger; anger a strong desire to physically attack and vanquish opposition. This hypothesis is strongly supported by the outward expression of fear and anger. Animals with no weapons for attack show no anger; animals that have no means of self-defence by muscular action show no fear. When a man in ordinary vocation is conducting a struggle for existence against his rivals, and when the contest is at its height, he may clench his fists, pound the table, perhaps show his teeth, and he may exhibit every expression of physical combat. Fixing the jaw and showing the teeth in anger merely

emphasize the remarkable tenacity of phylogeny. Although the development of the wonderful efficiency of the hands has led to a modification of the once powerful canines of our progenitors, the ancestral use of the teeth for attack and defence is still attested in the display of anger. In all stations of life difference of opinion may lead to argument, and argument to physical combat—even to the point of killing.

Physical violence of the savage and the brute still lies surprisingly near the surface. Although there is not convincing proof, still there is strong evidence that the effect of the stimulus of fear upon the body without physical activity is more injurious than the effect of fear with physical activity. It is well known that the soldier lying under fire awaiting in vain for orders to charge suffers more than the soldier that flings himself into the fray; that a wild animal in an open chase against capture suffers less than when cowering in captivity.

Civilized man may be said to be in a state of autocaptivity. The child has no desire to conform to the conventions of his elders, on the contrary, he naturally prefers to wear no clothes, to climb, to run, and play, and be dirty—to fight and hide and hunt and fish and kill according to the primitive design of his mind and body by his evolution through lower forms of life. It is such a commonplace that we scarcely realize the immense significance of the difficulty of the training of our children. For some twenty years the mother, the father, brothers, and sisters, friends, teachers, the community at large—even the policemen—are engaged in the difficult task of training and taming a child to the conventions and the work of his adult life. Even after this long period of taming and training this natural savage may in the end break out in many savage ways. The wild animals and primitive man have but little difficulty in bringing up their young in the ways designed for them by nature, but each generation of man must spend a prodigious amount of time in training its young for the obligations and duties of civilized life, then in time they do the same for the generations to follow—in other words, man exists in a state of autocaptivity, and this is a fact of great importance. In civilized life there is much restraint, little action, much emotion. An unexpressed slumbering emotion is measurably relieved by action. It is probable that the various energizing substances needful in physical combat such as the secretions of the thyroid, the adrenals, glycogen, etc., but which are not consumed in action may, if frequently repeated, cause physical injury to the body. That the brain is definitely influenced, even damaged by fear, has been proved by the following experiments:

Rabbits were frightened but not injured, and not chased by a dog. After various periods of time the animals were killed and their brain cells compared with the normal. Widespread changes

were seen. The principal gross phenomena expressed by the rabbit were rapid heart, accelerated respiration, prostration, tremors, and a rise in temperature.

The dog showed similar phenomena, excepting instead of muscular relaxation, as in the rabbit, it showed aggressive muscular action. Both the dog and the rabbit were exhausted, and although the dog exerted himself actively and rabbit remained physically passive, the rabbit was much more exhausted than the dog.

Other observations were made upon the brains of foxes chased for various distances by members of a hunt club, then finally overtaken by the hounds and killed. The brain cells of these foxes as compared with those of a normal fox showed extensive physical changes.

Man is capable of only such actions as his ancestors have through evolution—that is, phylogeny—made possible, and only by association. When an individual experiences such a contact with his environment that in his phylogeny would have led to action, but in him no physical action ensues, though there is widespread stimulation in preparation for action, this is emotion.

The effect of repeated stimulations of the emotions is seen in the destructive phenomena of worry, of fear, and, in a lesser degree, though analogous in principle, the phenomena of sexual love. In the case of a young woman with indigestion, insomnia, low spirits, loss of weight, and general loss of vitality and interest, who would venture to assert, in the absence of a correct history, of which she was the victim, some disease or a disappointment in love? Now in the history of cases of Graves' disease there is again and again given voluntarily or as an admission an account of some strong emotional stimulant—some deeply disturbing fact which thrusts itself upon the consciousness instantly on awakening—rather it awakens its victim in the course of the night and in the early morning; some dominating emotional stimulant which absorbs the attention during the day and disturbs the sleep in the night; the ever-recurrence of this evil stimulus is attended by an increase of all the emotional phenomena, so that gradually, indeed imperceptibly, the stimulus remains constant; the eyes protrude; the thyroid is enlarged, and full-blown Graves' disease is seen, a disease primarily involving the entire motor mechanism, or emotional mechanism.

The following is typical: A broker up to the panic of 1907 was in his usual health. During this panic his fortune and that of others was for almost a year in jeopardy, finally ending in failure. During this heavy strain he became increasingly more nervous, and imperceptibly there appeared a pulsating enlargement of the thyroid gland; an increased prominence of the eyes; marked increase in perspiration, even profuse sweating; palpitation of the heart; increased respiration, with frequent sighing; increase in

blood pressure; there was tremor of many muscles; rapid loss of weight and strength; frequent gastro-intestinal disturbances; loss of normal control of his emotions, and marked impairment of his mental faculties. He was as completely broken in health as in fortune.

These phenomena resemble closely those of fear and follow in the wake of a fear strain. In young women this disease often follows in the wake of disappointment in love; in women, too, it frequently follows in the wake of an illness of a child or parent in which the double strain of worry and of constant care are present. Since such strains usually fall heaviest upon women, they are the most frequent victims. In adolescent girls, when the innumerable stimuli due to the development of the sexual functions fall upon the thyroid and other glands, there is frequently observed an enlargement of the thyroid. Either iodine or thyroid extract in moderate doses will cause shrinkage of such a gland; but if these subjects in addition to their phylogenetic stimuli are subjected to unusual environmental stimuli, Graves' disease may develop.

Whatever the exciting cause of exophthalmic goitre, whether unusual business worry, disappointment in love, a tragedy, a strong fear, the illness of a loved one, an acute infection, overdose of iodine or thyroid extract, or of unknown cause, the symptoms are alike and closely resemble the phenomena of one of the great primitive emotions. Now, how could disappointment in love play a role in the causation of Graves' disease? If the hypothesis presented for the explanation of the genesis and the phenomena of fear is correct then it would hold for the emotion of sexual love. If fear is a phylogenetic physical defence or escape, but without resulting muscular action, then love is a phylogenetic conjugation without physical action. The quickened pulse, the leaping heart, the accelerated respiration, the sighing, the glowing eye, the crimson cheek, and many other phenomena are merely phylogenetic recapitulations of ancestral acts.

The thyroid gland is believed to participate in such physical activities, hence, it could well follow that many organs, including the thyroid gland of the disappointed maiden who is intensely integrated for a youth, will at every thought of him be subjected to a stimulation analogous to that which attended the ancestral consummation and under certain conditions it may inaugurate Graves' disease. Now, a happy marriage has many times been followed by a cure of the exophthalmic goitre which appeared in the wake of such an experience. The victims of Graves' disease present a counterpart of emotional exhaustion. The emotions in Graves' disease are abnormally powerful, as illustrated by personal observations of death from fear alone in several victims of this disease. Whatever the cause of this disease of the motor mechanism or the emotions the symptoms of Graves' disease are

the same; just as in fear, the phenomena are the same whatever the cause. In Graves' disease there seems to be a composite picture of an intense expression of the great primitive emotions. If Graves' disease is a disease of the motor mechanism or of the emotions, what is the source of the constant flow of stimulation that continues the disease? A stimulation that may be constantly present in waking and in sleep for months and years. The stimulus could scarcely be of nervous origin caused by environment alone, because the stimulus has a more even flow than environmental contact alone could possibly have. The following facts suggest that the thyroid gland plays the leading role of secondary stimulation: In suitable cases of Graves' disease if the activity of the thyroid gland is sufficiently decreased the phenomena of the disease are immediately diminished, and in favorable cases the patient is restored to approximately the normal condition. The heart slows, the respiration falls, the restlessness diminishes, digestive disturbances disappear, tremors decrease, there is a rapid increase in the body weight, and the patient gradually resumes his normal state. On the other hand, if to a normal individual extract of the thyroid gland is administered in excessive dosage over a period of time, there will develop nervousness, palpitation of the heart, sweatings, loss of weight, slight protrusion of the eyes, indigestion—in short, there will be produced, artificially, most of the phenomena of Graves' disease and of the strong emotions. On withholding the thyroid extract these phenomena may disappear. I use the qualifying word "may," because I have seen a number of cases of excessive administration of thyroid extract end in real Graves' disease. On the other hand, when there is too little or no thyroid gland the individual becomes dull and stupid and emotionless, though he may be irritable. This does not refer to those cases of hybrid myxedema due to a combination of the wreckage of Graves' disease and thyroid deficiency. The motor mechanism here is burned out. Hence, we see that the phenomena of the emotions may be, within certain limits, increased, or may be diminished, or abolished by increasing, diminishing, or totally removing the thyroid secretion. Graves' disease may be increased by giving thyroid extract and by any of the excitants of the emotions. It may be diminished by removing a part of the gland or by partially interrupting its nerve or its blood supply, or by physiological rest. Finally, in Graves' disease there is at some stage an increase in the size and in the number of the secreting cells of the thyroid gland.

The phylogenetic identity of physical injury and fear tells us why psychic shock is identical with traumatic shock; why in cases of exophthalmic goitre the psychic stimuli increase the phenomena of Graves' disease precisely the same as physical stimuli. Why the fear of operation causes the same exacerbation of all the symptoms as the physical injury of tissue in the course of

operation. Both physical injury and psychic stimuli cause a self-protective response which causes a stimulation of the motor or emotional mechanism. In Graves' disease, this mechanism being highly sensitized, the effect of either physical or psychic stimuli is immensely increased; hence, the startling effect of operation often seen. In Graves' disease there seems to be established a pathological stimulation of the entire motor mechanism of the human body. Its phenomena resemble continuous motion or at least a continuous primary stimulation of the entire motor mechanism. The nervous system alone is capable of initiating such a motor excitation, but as we have seen its continuation is effected through the agency of secondary influence—that of the activating ductless glands—especially the thyroid, which is the only gland whose secretion, wholly independent of the inauguration by the nervous system, is capable of equally stimulating the entire motor mechanism and of producing identical phenomena. By motor mechanism is meant the entire complicated machinery used in the production of physical action. The role of the thyroid is that of an activator. But the action of the thyroid, like the action of all the other organs of the body, is inaugurated either directly or indirectly by the nervous system. Environment, as Sherrington has said, drives the nervous system and the nervous system drives the entire organs of the body.

The question which next confronts us in a given case is this: What has caused the inauguration of the thyroid activity and what impels its continuation? Let us consider some of the conditions present and which seems to serve as exciting causes: It may follow an acute infection such as tonsillitis, or in the wake of an infectious disease, as measles, typhoid, etc.; it may follow large doses of iodine; administration of excessive dose of thyroid extract, especially if there is present a colloid goitre; overwork, especially in adolescence; worry; psychic shock and emotional disturbances. All these exciting causes produce a lowering of the threshold of the nervous system to stimuli and a diminution of the normal control of the brain. This statement is based on the clinical observation of hyperexcitability and the demonstration of actual lesions of the brain cells in each of the above-mentioned exciting causes; when the threshold is lowered, environmental stimuli will produce an increased activation of the brain, which in turn will drive to greater activity the various organs of the body, including the thyroid.

The impairment of nervous control by various diseases and nerve strain would expose the thyroid gland to abnormal stimulation. This stimulation in turn would increase the output of the activating thyroid secretion, the effect of which would be to further increase the excitability of the brain, or, in other words, would sensitize the brain. This reciprocal interaction may continue

until Graves' disease is evolved. The precise means by which this interaction is continued, that is, the physical chemical process by which it is wrought—is unknown, but it is known that this pathological interaction may be broken at either end—namely, by restoring to the brain its power of normal control, or by diminishing the output of thyroid secretions. If a case of Graves' disease can be so managed as to secure sufficient rest, secure a sufficient reduction of environmental stimuli, the disease may be arrested or cured. It is usually impossible to promptly enough disentangle this explosive vicious circle, and frequently the mere effort at cure becomes an exciting cause. If the brain could enter into the state of actual hibernation, like a bear, the disease would certainly be cured; but unhappily the knowledge of the gravity of the disease itself becomes one of the psychic excitants which aggravates the disease, the entanglement becomes frequently hopeless, and, like the Gordian knot, it must be cut. Although a widening experience confirms the value of surgical treatment of Graves' disease, there are still some who are not yet prepared to admit it.

Perhaps the strongest point of objection raised by those who oppose the phylogenetic hypothesis is that of admitting the benefits which follow surgery. While admitting the benefits of surgery they believe that these benefits are due to suggestion, to psychic influence. There are two points that answer this objection: (1) If psychic influences can cure the disease, then the surgeon alone possesses this remarkable influence, because all surgical cases have been unsuccessfully treated by internists first. This compliment to the superior psychic power of the surgeon, unhappily the latter cannot conscientiously accept, because the surgeon is unable to favorably influence his patient excepting at the time of his contact with the patient on the operating table, and at that time his patient is unconscious. Then again the surgeon has seen equal improvement in cases whose glands were removed without the patient's knowledge. (2) If it is asserted that the great benefits of surgery are due to psychic causes, then the disease may be produced by psychic influences which would be precisely in accord with our main hypothesis. Against this hypothesis are also urged the following: That in Graves' disease there is a condition of hypothyroidism not a hyperthyroidism. This statement is based on the following: The iodine content of the thyroid is diminished in Graves' disease; there are in severe cases sometimes symptoms of myxedema, and the favorable results of surgical treatment are due to psychic influences and not to the diminution of the thyroid secretion. As to iodine content, Beebe found iodine in every case analyzed by him, though in severe cases the iodine was diminished in quantity. Now, on the theory here proposed there is an enormous increase in the call for iodothyroid, and a decrease of this element in the gland should follow an increased

use of it. Then, as Beebe has pointed out, the iodine, like the bile salts, circulates from the gland to the body and returns again without being excreted. Now, in Graves' disease the thyroid is enormously vascularized, and the blood circulates through it in much larger quantity, which would afford a much increased facility for the circulation of iodine between the rest of the body and the gland; still further, the amount of colloid in which iodine is normally stored is much diminished in Graves' disease.

There is, too, experimental evidence that there is another activating substance besides iodothyron produced in the thyroid. This must be reckoned with, and finally, it must be borne in mind that in Graves' disease the body is highly sensitized to iodothyron just as it is sensitized to psychic and painful stimuli; hence, even a diminished amount might easily produce a harmful effect, just as even minor psychic or physical stimuli may cause harmful effects. Besides, the administration of either iodine or thyroid extract not only gives no relief in Graves' disease, but causes an increase in the symptoms. This strongly speaks against the disease as being due to a diminished thyroid secretion.

In the late stage of the disease in which there is a physical wreckage of most of the organs of the body, including the thyroid itself, from the body wide stimulation, there may be an odd mixture of myxedema and Graves' disease; the body is like the charred remains of a partially burned building, whatever is done toward salvage the fire extinguisher is no longer needed; the fire (Graves' disease) has burned itself out. Some of these cases are benefited by small doses of iodine or of thyreoglobulin, but the dose must be cautiously given.

We do not know why only certain of the vast number of individuals subjected to emotional stimulation, to nerve strain, to infections, and to the other factors acquire the disease. This problem is like that of explaining why only certain individuals become insane after nervous strain or after infections; why only some under strain develop cardiovascular disease, and so throughout the entire gamut of diseases the ultimate truth is not known; our problem is that of the exciting cause and cure. When the truth is known it will likely appear that some reduced factor of safety, such as a disproportion of inorganic salts, or some general metabolic change, accounts for the thin ice through which the exciting causes break.

Now, in cases of Graves' disease the mere proposal to perform an operation becomes also a pathological excitation; this excitation may so much increase the disease that the patient is even less able than before to bring herself to submit to adequate treatment. On all sides this disease is beset by vicious circles, by pathological interactions. The ideal plan of approach, at least in my experience, is to assure the patient that hers is a curable

malady, that it can be treated in a hospital, and that non-operative measures will first be tried; then if they prove inadequate a simple operation will be done, that it will be best to leave this decision to the judgment of her medical adviser, and that since even the discussion of operation is both unpleasant and injurious, it would be best not to open this subject again. The patient usually gladly consents to leaving the whole matter to the judgment of the physician, and the way is then opened for the most effective treatment which in my judgment has ever been proposed—namely, ligation or excision on the new principle of *anociassociation*.

The anesthetist, a nurse, specially trained, gives fictitious inhalations under the precise conditions of regular anesthesia under the guise of "inhalations" supposed to be a part of the general treatment. Every morning the patient is given a sterile hypodermic. On the morning of the operation, which is performed in one of the favorable phases of the numerous cycles of the disease (on the morning of the day of the operation), the hypodermic will contain morphine and seopolamine, and instead of an oxygen "inhalation," nitrous oxid is added and the patient falls to sleep in her bed without the slightest knowledge or suspicion that the first step of an operation had already begun. The patient is then transported anesthetized to the operating room, where the operative field is prepared. Up to this point the patient's brain, hence, the remainder of the body, is in a negative state, and this is half of the innovation of the specialized operation; the other half is this, any injury of any sensitive part of the body, though the patient is under inhalation anesthesia, excites the brain, and hence through the brain all of the motor mechanism, especially the thyroid. Inhalation anesthesia is but a thin veneer, and although the patient is unconscious, the afferent impulses set up by the operation reach the brain apparently as readily as if no anesthesia were given.

This is the source of the hyperthyroidism, so-called, that constitutes the greatest danger of the operation. Operation under inhalation anesthesia on any sensitive part of the body produces precisely the same exacerbation of the disease (hyperthyroidism) as operations upon the thyroid gland itself. How may this be avoided? It may be wholly avoided by the use of complete local anesthesia, by the use of novocaine throughout the entire operation, just as completely as if the patient had received no general anesthesia. The patient has received no psychic stimulation arising from knowledge of the imminence of the operation, and none in being anesthetized, and finally, no afferent impulse reaches the brain from the field of operation—then not a single nocuous or harmful impulse reaches the brain—this state can be designated only by coining a new word, *anociassociation*. The result of operations performed by this method is scarcely credible; the condition of the patient at the end of the operation is precisely the same

as when in bed the day before. Indeed, this is the standard; unless the result equals this, there has been an error in the technique.

By this technique the scope of the operation is greatly increased, and the gland can be safely removed from any patient whose condition will endure the metabolic influence of the sudden withdrawal of so much active gland tissue. In such cases it is best to ligate the poles and later, if necessary, excise the lobe. This operation of pole ligation is done in bed without the patient's knowledge and in a few minutes.

In any case the operation is but a means to the end—namely, the raising of the threshold of environmental stimuli by diminishing the amount of activating sensitizing thyroid secretion and in conjunction with physical and psychic rest, permitting the patient to regain the power of normal control by the brain. Travel, diversion, nature, all are helpful, the operation serving to break the pathological change at one of its strongest links. These patients should be and can be literally taken by the hand and led away from mankind through the flowery paths of ease and pleasure to the haven of health.

SUMMARY. Graves' disease is not a disease of a single organ or the result of some fleeting cause, but is a disease of the motor mechanism of man, the same mechanism that causes physical action and that expresses the emotions; its origin is in phylogeny and its excitation is through either some stimulating emotion intensely or repeatedly given, or some lowering of the threshold of the nerve receptors, thus establishing a pathological interaction between the brain and the thyroid. This pathological interaction may be broken by diminishing the thyroid output, thus allowing the brain to regain normal control, or by securing physiological rest, which simultaneously secures normal control of the brain, which in turn will give the thyroid the opportunity of returning to the normal.

As to the effect of the operation of excision of a lobe or of ligation, the benefits are so striking and so uniformly successful in cases which are the despair of medicine that that point is settled beyond doubt. Because the conception here presented relates wholly to the release of energy it is designated the Kinetic Theory.

THE COMMONER FORMS OF RENAL DISEASE, WITH SPECIAL
REFERENCE TO THE KNOWLEDGE OF THEM MOST
USEFUL AT PRESENT TO THE GENERAL
PRACTITIONER¹

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INTRODUCTION.

EVERY man in general practice sees, from time to time, patients suffering from renal disease. In my own experience, and, I believe, in the experience of many medical men, it has become clear that as regards the diagnosis of renal disease, mistakes are made in four main directions: (1) Serious renal disease, when present, may be entirely overlooked. (2) Urinary changes, due primarily to disease of other parts of the body, notably of the heart and arteries, may often be wrongly interpreted as evidences of primary renal disease. (3) There is an attempt among some to push the diagnosis of the exact form of renal disease present to a point beyond that to which we are, in reality, able safely to arrive by the clinical methods which have as yet been worked out. (4) More, perhaps, err on the other side and do not try to distinguish the different forms of renal disease, even when distinctions can easily and profitably be made among them clinically; thus, too often, do we find all renal diseases lumped together as "nephritis," no attempt being made to separate the degenerative, inflammatory, and circulatory nephropathies from one another or to ascertain the toxic or infectious etiological factors. Now, during the last ten years, especially, clinicians and pathologists have been working vigorously at the problems connected with renal disease, and certain real advances in our knowledge of these conditions have been made. Among the many studies which have been prosecuted and the results which have been achieved, I shall attempt, to make a selection of certain points which seem to me of greatest interest, and of greatest value, to men who are actually engaged in the practice of medicine. I shall pay most attention to: (1) The symptoms which indicate the existence of renal disease or which lead us to suspect it; (2) the commoner forms of renal disease clinically grouped; (3) the pathological anatomy of the commoner forms of renal disease; (4) the main etiological factors concerned; (5) the influence of experimental injuries to the kidneys on our conceptions of renal disease; (6) the conception of renal diseases based on

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the chemistry of the colloids; (7) certain functional tests for renal efficiency; and, (8) in closing, some therapeutic principles based on our present knowledge of renal disease.

SYMPTOMS WHICH INDICATE THE EXISTENCE OF RENAL DISEASE, OR WHICH LEAD US TO SUSPECT IT.

Under this caption I shall refer to (1) certain urinary changes; (2) the occurrence of edema; (3) certain vascular changes; and (4) certain phenomena referable chiefly to an intoxication of the nervous system, the so-called uremic symptoms.

The urinary changes to which I refer include (1) albuminuria; (2) cylindruria, or the presence of casts in the urine; (3) changes in the amount of urine (polyuria or oliguria); (4) nycturia, or rising at night to pass urine; (5) so-called hyposthenuria, the condition in which the kidney is no longer able to secrete a concentrated urine, rich in metabolic products and salt, the twenty-four hours' urine having, constantly, a lower specific gravity than normal; and (6) hematuria.

As is generally known, *albuminuria*, by itself, need not point to renal disease, for albumin may appear in the urine in various inflammatory affections of the lower urinary passages (pelvis of the kidney, ureter, urinary bladder, urethra); in such cases, pus is also present in the urine (pyelitis, cystitis, gonorrhea). In women, a leucorrheal discharge from the vagina, or menstrual blood, may be mixed with the urine and simulate an albuminuria. Even when the albumin comes from the kidney (true renal albuminurias) we have to distinguish between those due to serious renal disease, or to severe cardiac insufficiency, on the one hand, and those of very little clinical import, the so-called physiological albuminurias, including cyclic albuminuria and orthostatic albuminuria, on the other; in the latter group there may be an entire absence of other signs of renal disease (casts in the urine, heart hypertrophy, arterial hypertension, etc.).

The heat and acetic acid test and the cold nitric acid ring test suffice for all ordinary clinical purposes; for a quantitative estimate of albumin, a judgment based upon the precipitate obtained with the heat test may be accurate enough, though the estimation by Esbach's albuminometer is easily carried out.² It is generally believed that the albumin is given out by the glomeruli, not only

² In rare cases we are surprised to find a urine in which, on heating, an abundant precipitate of albumin occurs, while on heating longer, and to a higher temperature, the precipitate again goes into solution, to fall out once more on cooling. Should the physician meet with such a urine, he will know at once that he is dealing with the so-called Bence-Jones body in the urine, and he may feel sure his patient is suffering from some form of disease of the bone marrow, in all probability, myeloma. An x-ray examination of the bones in such cases will reveal the size and distribution of the tumors.

in glomerulonephritis, but also in renal diseases in which the glomeruli look histologically normal (for example, nephropathy of pregnancy).

The occurrence of *casts* in the urine (cylindruria) is of great help in indicating that an albuminuria is truly renal in its origin. Contrary to what we were long taught, however, the kinds of casts present (hyaline, granular, waxy, etc.), while easily differentiable from one another microscopically, are not of much help in distinguishing the various forms of renal disease from one another; an exception must be made in the case of blood-casts (*vide supra*).

A marked diminution or a great increase in the quantity of urine passed (oliguria, polyuria) always excites our suspicion regarding the function of the kidneys and should lead to a careful examination for other signs and symptoms of renal disorder. An *oliguria*, associated with albuminuria and cylindruria, and, especially, associated with hematuria, is a common symptom in organic renal disease, particularly in certain diseases of the glomeruli (for example, glomerulonephritis). But we should never forget that in failing heart the interference to the circulation in the kidney may lead to marked oliguria with albumin and casts in the urine, and that these signs may disappear entirely when the circulation has been restored and the stasis in the kidney done away with.

A persistent *polyuria*, with urine of low specific gravity, is often a sign, either of contracted kidney, or of diabetes insipidus. Polyuria also occurs in amyloid disease of the kidney, and in pyelitis. A polyuria with high specific gravity of the urine is rarely seen in renal disease; it is, of course, most often met with in diabetes. Temporary polyurias occur very frequently in a variety of conditions (for example, after drinking water; on the disappearance of an edema; in convalescence from acute disease; after taking diuretics).

In recording the history of a patient, it is always well to ask the question. "Do you have to get up at night to pass urine, and if so, how many times?" for this symptom (*nycturia*) is very common in renal disease, especially in beginning contraction of the kidney.

The term *hyposthenuria* I have already defined. The symptom is not often recognized in general practice, for, to observe it, the whole twenty-four hours' urine has to be collected, repeatedly, and the specific gravity thereof regularly taken. According to Schlayer, such a secretion of thin urine, hyposthenuria, can arise in two ways: either through lessened production of solid substances, or through increased production of water. In the first instance, the hyposthenuria appears to be due to an injury to the cells of the renal tubules; in the second instance, to an oversensibility of the renal vessels, Schlayer and his pupils speak, therefore, of a *tubular* and of a *vascular hyposthenuria*. The distinguishing characteristics of these two hyposthenurias are briefly these: In the tubular form,

the concentration remains permanently the same; it is always low. The addition of common salt to the food does not heighten the specific gravity, and the total amount of sodium chloride given out in the twenty-four hours cannot be increased by feeding common salt, since the tubules do not work adequately. In the vascular type, the concentration also remains permanently at the same height, but the specific gravity may be much higher than in the tubular type. Here, an addition of sodium chloride is quickly eliminated with increased output of water, but the concentration remains the same. The renal vessels, here, appear to be over-sensitive and to react to every secretory stimulus by producing larger amounts of water.

Renal *hematurias* (with formation of blood casts) are of considerable diagnostic importance, for they point definitely to diseased glomeruli. The glomerular affection may be either a diffuse glomerulonephritis due to soluble toxins in the blood, or a focal embolic injury of single glomeruli or single capillary loops in glomeruli due to bacterial emboli (*e. g.*, in endocarditis lenta, in sepsis with acute tonsillitis, and in other infections with bacteriemia).

Whether an *edema* is due to renal disease or to cardiac insufficiency or to some other cause (angioneurosis, anemia, cachexia) is sometimes hard to determine. The edema of renal origin seems to depend upon two factors: (1) upon an injury to the bloodvessels of the glomeruli of the kidney itself, either obstructing their lumina, or interfering with their capacity for contraction and dilatation, and preventing the excretion through the kidney of common salt and water in proper amounts; and, (2) a lesion of the small bloodvessels all over the body (especially of the skin and of the subcutaneous tissue), leading to increased permeability of the same. In contrast to the edema due to stasis (chronic heart disease), in which the influence of gravity, and distance from the heart, play a great role in the distribution of the edema, the edema of renal origin begins very often in the face, especially about the eyelids. A fact which is often overlooked is this: *the edema which occurs in the late stages of contracted kidney is rarely directly due to the renal lesion itself but is a true stasis edema due to beginning failure of the heart.* Now and then, in the course of contracted kidney, an edema directly renal in origin occurs, owing to the superimposition of an acute renal disease upon the chronic disorder.

The occurrence of *high blood pressure* (arterial hypertension) with *hypertrophy of the left ventricle* are very important signs and often lead us to investigate the functional power of the kidneys. A systolic blood pressure of 160, 180, or more, associated with hypertrophy of the left ventricle (apex beat displaced, downward and outward) should always make one think of the possibility of contraction of the kidney. We meet with such hypertension and cardiac hypertrophy especially often in patients of middle life who have

indulged freely in food and drink, though we sometimes see them also in abstemious individuals. In the absence of other factors accounting for the hypertension and the cardiac hypertrophy, one can be fairly sure that the condition is due to an atherosclerotic disease of the fine arterioles (in the sense of Jores) supplying the various organs of the body, including the kidneys, and leading, in the latter, to some contraction of the same. There may be only a trace of albumin in the urine with a few casts, the specific gravity is usually rather low; and the patients give, usually, a history of nycturia, sometimes lasting for years. The complaint of the patient on consulting the physician, however, is usually one dependent on the hypertension, or on the beginning cardiac insufficiency (headache, dizziness, dyspnea, fatigability, etc.).

It would appear that arterial hypertension with cardiac hypertrophy, in renal disease, may occur whenever the process of urinary secretion is largely interrupted throughout its whole cross-section, in any part of the kidneys, for example, (1) in diffuse glomerular nephritis, (2) in sublimate poisoning with diffuse necrosis and blocking of tubules, (3) in most contracted kidneys, especially in those due to atherosclerosis of the vasa afferentia.

The so-called *uremic symptoms*, referable to an intoxication of the central nervous system (headache, dizziness, vomiting, diarrhea, renal asthma, somnolence, disturbances of visions from albuminuric retinitis, convulsions, coma) may sometimes though rarely be those which lead the patient first to consult the physician. Unless a thoroughly systematic examination were made in such a case as a matter of routine, including an examination of the urine, and of the blood pressure, the cause of the nervous symptoms might be entirely overlooked, or wholly erroneously interpreted.

THE COMMONER FORMS OF RENAL DISEASE, CLINICALLY GROUPED.

If we leave out pyelitis, on the one hand, and chronic passive congestion (stasis) of the kidneys, on the other, the forms of renal disease commonly met with by the general practitioner may be subdivided into three great groups.

I. Cases of acute renal disease (or nephropathy), with or without, dropsy.

II. Cases of subacute or chronic renal disease (or nephropathy), with true "renal" edema occurring in their course.

III. Cases of chronic renal disease (or nephropathy), without "renal" edema, lasting perhaps for years.

The first group of cases are often designated as "*acute Bright's disease*," a scoop-net which includes a large variety of renal diseases histologically and etiologically very different from one another (for instance, embolic purulent nephritis, ascending purulent nephritis, acute glomerulonephritis, acute tubular degenerations, etc.).

Form of disease.	Amount of urine.	Color	Specific gravity.	Amount of albumin.	Sediment.	Duration.	Results, accompaniments, etc.
Stasis kidney.	Scanty.	Dark.	High	Slight or moderate	Urates; occasional casts and red blood cells.	As long as stasis lasts.	Cardiac death; infarctions.
Acute nephropathy.	Oliguria or anuria; rarely polyuria.	Dark, occasionally bloody	High to normal.	Usually large.	Abundant; red blood cells; white blood cells; granular, hyaline, blood and epithelial casts.	Weeks to months.	Uremia common; sometimes arterial hypertension; edema common.
Chronic nephropathy with renal dropsy (chronic parenchymatous nephritis).	Oliguria.	Dark.	High.	Large.	Abundant; all varieties of casts; fatty epithelium; red blood cells.	Death, a few months to one or two years; rarely healing with secondary contraction of kidney.	General anasarca. Heart hypertrophy. Usually increased blood pressure. Uremia common.
Chronic nephropathy without renal dropsy (contracted kidneys, most often arteriolar nephropathy).	Polyuria.	Pale.	Low, usually	Trace.	Very little; occasional cast or red blood cell.	Years; decades.	Progressive arterial hypertension to 220 or 260 or more; cardiac hypertrophy; no dropsy until myocardial insufficiency sets in. Death from apoplexy, uremia, cardiac failure, or, often, terminal infections.
Amyloid.	Normal or polyuria.	Pale.	Normal or low.	Variable; often much.	Slight; hyaline, granular, and waxy casts.	Months to years.	Marked edema usually; no uremia; normal blood pressure; no heart hypertrophy; chronic suppuration, tuberculosis or lues as etiology.
Pyelitis.	Normal or polyuria.	Turbid.	Normal or low.	Slight.	Pus cells; pelvic epithelium (casts only when complicated by pyelonephritis or other nephropathy).	Acute or chronic.	Fever; pain; etiology may be evident.
Cystitis.	Normal or oliguria.	Turbid, sometimes bloody.	Normal.	Slight, due to pus.	Slight; pus cells; red blood cells; squamous epithelium; triple phosphates.	Acute or chronic.	Alkaline urine; ammoniacal odor; complicated often by pyelitis and pyelonephritis.

The second group includes the cases often described as "*subacute Bright's disease*" or as "chronic parenchymatous nephritis" (large white and large variegated kidney).

The third group includes the *contracted kidneys*, not only the so-called "genuine" or "primarily contracted kidney" but also the so-called "secondarily contracted kidney" (see notes on pathology).

In the preceding table the characters of the urine, duration of the disease, the results, etc., are summarily tabulated.

NOTES ON THE PATHOLOGICAL ANATOMY AND HISTOLOGY OF THESE COMMONER FORMS OF RENAL DISEASE.

The kidneys are perhaps the most important excretory organs of the body and they are frequently subject to injury. The injuries sustained vary in kind and degree according to the quantity and quality of the injuring agent, and its mode of entrance into, and exit from, the kidneys.

Each kidney must be thought of as a very complicated organ, made up of a whole series of *secretory units*, each unit consisting of its glomerulus and attached tubule (*parenchyma*), surrounded by bloodvessels and a certain amount of connecting tissue pertaining to that glomerulus and tubule and filling up the *interstices* between neighboring secretory units. Since single parts of the secretory unit and of the interstitial tissue may be separately diseased, the most variable clinical and pathological pictures arise. The study of renal diseases is made more complex by the fact, that, after an injury has been sustained, healing processes may go on for years; after death, we may see only the scars of some old process and be unable to form an accurate judgment as to the cause and course of the disease which preceded the scars.

The older pathological literature is permeated by the terms "interstitial" and "parenchymatous" diseases of the kidney. By the former, is usually meant involvement of the bloodvessels and the connective tissue of the organ; by the latter, involvement of the glomeruli and tubules themselves. Now, when patients suffering from acute disease of the kidney die and come to autopsy, it is sometimes clearly evident that the parenchyma, sometimes just as obvious that the interstitial tissue, has suffered predominantly; in chronic renal disease, where reparative processes have been going on for a long time, it is rare to find a process which is purely "interstitial," on the one hand, or purely "parenchymatous," on the other; both parenchyma and interstitial tissue have undergone alterations in varying degree.

One very important distinction among the pathological processes which occur in the kidney is that which divides them into *focal*

(scattered, or disseminated) lesions, on the one hand, and diffuse (widespread, almost universal) lesions on the other. In general, the more diffuse the renal disease, that is to say, the greater the area of kidney substance injured, the greater the danger of death in acute processes, and of early renal insufficiency should the patient live long enough for repair to set in. The disseminated (or focal) lesions, on the other hand, may cause very few symptoms at the time of their occurrence in the acute stages of the disease, and, when they go on to the healing stages, sufficient healthy renal tissue may remain to permit them to work fairly efficiently for a long time.

The processes described by pathologists as "interstitial" are most often due to disseminated or focal lesions, while the processes described by them as "parenchymatous" (glomerulotubular) are most often due to diffuse lesions. This makes it easy to understand why it is that patients with predominantly interstitial lesions may apparently recover entirely from a renal injury, or may live many years, without disturbing symptoms; whereas, in patients with predominantly glomerulo-tubular lesions, the prognosis is worse. As Aschoff and others point out, however, this is only a general rule, for if a diffuse injury affect only the epithelium of the renal tubules, leaving the glomeruli and bloodvessels intact, or nearly so, the organ may, by a regenerative process, become entirely normal again, provided the patient survive the acute insult. But extensive diffuse injury to the glomeruli seems rarely, if ever, to be wholly recovered from; it leads easily to permanent insufficiency of the kidneys, though, compensatory processes may be advantageously operative, for a time, before the final decompensation sets in.

The attempts which have been made sharply to distinguish *glomerular* lesions from *tubular* lesions, in diseases of the renal parenchyma, are praiseworthy and have undoubtedly enriched both clinical and pathological knowledge. But we must keep ever in mind the fact, that, on the one hand, loss of epithelium often leads to proliferative changes in the connective tissue which constricts the tubules and causes retention cysts with atrophy of glomeruli, while, on the other hand, an injury destroying a glomerulus can lead to "inactivity atrophy" of a tubule, and when we recall the various regenerative and hypertrophic processes which may complicate the histological picture in chronic cases, it is easy to see how difficult to decipher a given end stage may be. We can only be grateful that men like Councilmann, Christian, Dickson, Ewing, MacNider, Mallory, Ophüls, Pearce, Welch, and Winternitz, in this country, and Aschoff, Herringham, Thursfield, Heineke, Jores, v. Kahlden, Langhans, Löhlein, Reichel and Ribbert, in Europe, have done, and are doing, so much to solve the histological difficulties by which we are confronted. From what I have said regarding parenchymatous and interstitial lesions, regarding

injury to the glomeruli and harm to the tubules, and concerning focal and diffuse processes, involving these organs, it is obvious that the unravelling of a process by histological study can be no easy task.

The time has come, I think, when clinical men and pathologists should be very cautious in the use of the word "nephritis," since if in accordance with the best usage at present, we limit the meaning of this word definitely to inflammations of the kidney, the term "nephritis" is by no means synonymous with the term "renal disease" or "nephropathy." The latter is a much more inclusive term, embracing, as it does, not only inflammation of the kidney (nephritis), but also any disease of the kidney, be it inflammatory, degenerative, or circulatory in origin.

Let us take the diffuse hematogenous nephropathies, that is, the diffuse renal diseases due to some noxa brought to the kidneys by the blood, as an example. In one set of them, the tubules of the kidneys are chiefly affected, the glomeruli being much less or not at all involved. Here we have to deal with a toxic degeneration of the epithelium of the renal tubules, rather than with an inflammation (nephritis). Examples of such toxic necroses, or degenerations, of the renal tubules are seen in the kidney of phosphorous poisoning, that of corrosive sublimate poisoning, and the renal disease which occurs in pregnancy. On the other hand, a soluble poison brought to the kidneys by the blood may cause true inflammation of nearly all the glomeruli of the kidney, the so-called "glomerulonephritis." A typical example is the severe form of acute nephropathy which so often complicates scarlet fever.

The toxic degenerations of the renal epithelium, though giving rise to acute nephropathies, need not necessarily be fatal. Indeed, if the intoxication cease, the patient may recover completely. This is especially true of the intoxication of the kidney which sometimes occurs in pregnancy. As soon as the uterus is emptied, the intoxication ceases and the patient as a rule recovers promptly. In cases of cure after necrosis of the epithelium in sublimate poisoning, the epithelium of the kidney is regenerated.

Every practitioner is familiar with patients who have had acute renal disease and recovered. We have to distinguish carefully, however, those who become entirely well, from those who only apparently get well, but who, actually, still have progressive lesions and who succumb, later on, to chronic renal disease. In the latter cases, we have to deal, in the acute attack, usually, with milder forms of glomerulonephritis, associated with a tubular injury, in which recovery is incomplete, the reactive processes leading gradually to a "secondary contraction" of the kidney. Many acute, focal, inflammatory lesions doubtless heal and never give rise, either in the acute stage, or during the period of repair, to any serious symptoms.

In the cases of our second clinical group, so-called subacute

Bright's disease or chronic parenchymatous nephritis, we have to deal nearly always with extensive glomerulonephritis, with tubular degenerations, combined with extensive processes of repair. The inflammatory and reparative processes are diffuse. There are two groups of cases: (1) that in which there is marked desquamation and proliferation of epithelium and capsule of the Malpighian tufts ("stormy type" of Löhlein; desquamative type of v. Kahlden) and (2) that in which the phenomena mentioned are not prominent, the histological changes consisting chiefly of enlargement of the glomeruli, the loops of which are crowded with cellular elements of the endothelial type ("milder type" of Löhlein; thrombosing type of v. Kahlden; intracapillary glomerulitis of American writers). Such subacute, diffuse, inflammatory, nephropathies lead, usually within a year or two, sometimes in a month or two, to a fatal termination; in rare instances, where the injury has been less complete, there may be gradual healing with secondary contraction of the kidney; then the patients may live for years without troublesome symptoms, until, later on, uremic symptoms appear, or cardiac failure sets in.

Recent studies have thrown much light upon the nature of the different forms of "contracted kidney." The contracted kidney is always the end-stage of some earlier process, and we know now that a series of processes, entirely different from one another in the beginning, may give rise to similar end-stages, namely, contracted kidneys. It would seem probable, from newer studies, that only in a small percentage of the cases are contracted kidneys to be regarded as the end-stage of a preceding nephritis. I mean, of a glomerulonephritis. Occasionally, too, contracted kidneys result from an earlier embolic (focal) nephritis, or from the healing of an interstitial nephritis (Aschoff). But there is growing evidence for the belief that many contracted kidneys are renal atrophies of circulatory origin, due to *atherosclerosis of the small arterioles supplying the kidney*; it is thought that this arteriolar-sclerosis, a part of a process affecting the organ-arterioles generally throughout the body, leads to lessened blood supply to great numbers of glomeruli, to hyaline degeneration of the same and to inactivity atrophy of the corresponding tubules—the totality of changes accounting for the gradual shrinking of the kidney. This form of contracted kidney, some authors assert, should not be regarded as a "nephritis" at all, but as an atrophic nephropathy, the result of arteriolar change.

There is another form of atherosclerotic kidney in which, owing to severe atherosclerotic disease of single arterial stems, there is "patchy" atrophy and contraction, with very coarse granulation of the surface of the kidney (Ziegler); this form is that usually spoken of in the text-books as the "atherosclerotic kidney," while the disease described above as probably due to atherosclerosis of the small organ arterioles rather uniformly throughout both

kidneys, is usually referred to, in the text-books, as "genuine contracted kidney." This conception of "genuine contracted kidney," championed especially by Jores and his pupils, would seem to be a return to the English idea, advanced years ago by Gull and Sutton and later supported and extended by Johnson, that contracted kidneys are the result of "arterio-capillary fibrosis." The changes in the small arteries of the organs can be made out even in cases of beginning contraction of the kidneys, in middle and later life, in which death has occurred from cerebral hemorrhage, after a period of extreme arterial hypertension with cardiac hypertrophy (Löhlein).

FACTORS CONCERNED IN THE ETIOLOGY OF THE COMMONER FORMS OF RENAL DISEASE.

From the etiological side we may divide the renal discases or nephropathies into two great groups: (1) Those due to injuries reaching the kidneys through the blood, the so-called *hematogenous* or *descending nephropathies*, and (2) those due to injuries reaching the kidneys through the urine, the so-called *urinogenous* or *ascending nephropathies*.

The hematogenous nephropathies may, in turn, be divided into (a) those which are *diffuse* and (b) those which are *focal*. The former are due to soluble toxic substances circulating in the blood, the latter to organized particulate substances, namely bacteria.

The *diffuse hematogenous nephropathies*, due to soluble toxic substances, are further analyzable on the etiological side, and here it is interesting that the different soluble toxins seem to be to a certain extent, selective, regarding the particular structures of which the kidney is made up. Thus one set of toxins picks out the epithelial cells of the tubules, another has a selective effect upon the glomeruli, and a third group, apparently, upon the small arterioles of the organs, especially upon the vasa afferentia.

Tubular degenerative nephropathy may be due to a whole series of soluble poisons, including corrosive sublimate, phosphorus, potassium bichromate, the poisons produced in the uterus of the pregnant woman, the toxins of cholera, yellow fever, and of other acute infections, and hemoglobin.

The sublimate kidney has been carefully studied by A. Heineke, the phosphorus kidney by Landsteiner, the pregnancy kidney by several observers, the cholera kidney by E. Fraenkel, the yellow fever kidney by Councilmann, and by Marchoux and Simond, and the hemoglobin kidney by J. E. Schmidt.

The toxic affections of the glomeruli (*glomerulonephritides*) may be acute, subacute, or chronic and may be of the desquamative (or catarrhal) form, or of the intracapillary (or thrombosing) form. But in all cases, the commonest etiological factor seems to be a

streptococcus toxin. This form of nephropathy is most common after scarlet fever, tonsillitis, and other forms of streptococcus infection. It would appear that the toxins in pneumococcus infection, and in typhoid fever, can sometimes cause a glomerulonephritis. In Löhlein's series, by far the commonest etiological factor was preceding streptococcus sore throat. It is not improbable that the glomerulonephritis which sometimes complicates diphtheria, tuberculosis, dysentery, and certain other infections may be due to complicating streptococcus infection, with absorption of streptococcus toxins into the blood, through which they reach the glomeruli. The frequency of this form of nephropathy following exposure to cold may stand in relation to streptococcus sore throat. In the outspoken forms of so-called parenchymatous nephritis, where there is a combination of glomerulonephritis with degenerative tubular nephropathy, the same etiology (streptococcus toxin) seems to be commonest.

Whether the arteriolar nephropathy, which gives rise to the genuine contracted kidney, depends upon the action of soluble toxins upon the vasa afferentia directly, or is secondary to an arterial hypertension, which in turn is kept up by some general intoxication, is not yet satisfactorily known. The relation of this form of arteriolar disease to the excessive use of food and alcohol, is interesting.

If we turn now to the etiology of the *focal hematogenous nephropathies*, we shall find that they depend upon bacteriemias, with lodgement of single bacteria or groups of bacteria, in the kidney substance, namely in individual glomerular loops, in blood capillaries among the renal tubules, or passing through these, in the interstitial tissue of the kidney, or by excretion into the kidney tubules, where multiplying, they may form bacterial casts.

At least two forms of *embolic nephritis* can be distinguished—an embolic purulent nephritis, due to streptococci, or staphylococci, and an embolic, hemorrhagic (non-purulent), glomerulonephritis, due to embolism of single bacterial loops in the glomeruli by the streptococcus viridans in endocarditis lenta.

What the organism is in the acute interstitial nephritis which Aschoff has described after scarlet fever, in which the cellular exudates consist of cells resembling lymphocytes, is not known. The excretory form of hematogenous bacterial nephritis has been especially studied by Orth. Here the bacteria reaching the kidney by way of the blood may be excreted through the glomeruli, or perhaps through the tubules, into the lumina of the tubules, where they may multiply and give rise to bacterial casts. As the urinary flow is slowed in the portions of the tubules situated in the medulla of the kidney, these casts are found in that region, and the soluble toxins that the bacteria produce give rise to necroses and purulent inflammations near the apex of the pyramid; hence the name given by Orth to this form of nephropathy (nephritis papillaris mycotica).

The *urinogenous or ascending nephropathies* are divisible into two great groups (a) the hydronephrotic nephropathies and (b) the pyelonephritides.

The hydronephrotic nephropathies are due to pressure of urine owing to obstruction in the urinary passages (renal calculus, ureteral obstruction, prostatic hypertrophy, stricture of the urethra, etc.). Such hydronephrotic nephropathies may, obviously, be either unilateral, or bilateral, according to the seat of the obstruction.

A pyelonephritis may be due to any one of the pyogenic organisms, though it is most often, perhaps, dependent upon the *Bacillus coli communis*. Not infrequently the tubercle bacillus is the cause, and, in some cases, we have mixed infections of tubercle bacilli and pyogenic microorganisms.

In the following table I have tentatively classified the commoner forms of nephropathy, according to their pathology and etiology:

I. RENAL DISEASES DUE TO INJURIES REACHING THE KIDNEYS THROUGH THE BLOOD (HEMATOGENOUS, OR DESCENDING NEPHROPATHIES.)

A. *Diffuse hematogenous nephropathies* due to soluble toxic substances.

(a) Tubular degenerative nephropathies (*e. g.*, sublimite kidney; phosphorus kidney; bichromate kidney; pregnancy kidney; hemoglobinuric kidney; kidney of cholera, yellow fever and other acute infections).

(b) Glomerulonephritis (acute, subacute, chronic), due most often to streptococcus toxins.

(1) Catarrhal form with desquamation and proliferation of capsular epithelium.

(2) Intracapillary or thrombosing form of glomerulitis.

(c) Arteriolar nephropathy (chronic), probably due to action of toxic substances on organ arterioles, causing atherosclerosis of vasa afferentia.

B. *Focal hematogenous nephropathies* due to bacteriemias.

(a) Embolic (purulent) nephritis from streptococcus and staphylococcus.

(b) Embolic hemorrhagic (non-purulent) glomerulonephritis (large red or variegated kidney due to streptococcus viridans).

(c) Acute interstitial nephritis with lymphocytic exudate after scarlet fever.

(d) Excretory bacterial nephritis (*nephritis papillaris mycotica* of Orth) (casts of cocci).

II. RENAL DISEASES DUE TO INJURIES REACHING THE KIDNEYS THROUGH THE URINE (URINOGENOUS, OR ASCENDING, NEPHROPATHIES).

- (a) Hydronephrotic nephropathy (due to obstruction in urinary passages) depending on renal calculus, ureteral obstruction, prostatic hypertrophy, stricture of urethra, etc.; may be unilateral or bilateral.
- (b) Pyelonephritis.
 - (1) Pyogenic.
 - (2) Tuberculous.

THE INFLUENCE OF EXPERIMENTAL INJURIES TO THE KIDNEYS ON OUR CONCEPTION OF RENAL DISEASES.

Most hopeful for our future knowledge of renal disease is the increasing tendency to solve the problems connected with them by resorting to experiment. During the last ten years, the results of many researches, thus specifically directed, have been reported, and not only has our knowledge of the pathological anatomy and histology of renal disease been furthered, but also that concerning the function of individual parts of the kidney and the way these functions are disturbed in lesions of different kinds, have been increased in a most gratifying way. New light has been thrown upon the functions of the glomeruli on the one hand, and upon the tubules on the other, and we are rapidly getting a clearer insight into the nature of renal edema, of oliguria, of anuria, of polyuria, and of the relations of renal disease to arterial hypertension, to cardiac hypertrophy, and to uremia.

I can scarcely do more than direct attention to the bare outline of the work that has been undertaken and accomplished. To those who are interested in following the subject further, I can heartily recommend the perusal of Dr. Richard M. Pearce's Harvey Lecture on "Experimental Nephritis,"³ in which the subject is presented in a particularly clear and illuminating manner, and where full references to the bibliography are to be found. To those who rejoice at the progress of medical research in America, it is especially satisfactory to find so many American names among the contributors on the experimental side: H. A. Christian, E. C. Dickson, H. Emerson, M. C. Hill, T. C. Janeway, Jr., G. Lyon, S. J. Meltzer, W. Ophüls, R. M. Pearce, J. H. Austin, A. B. Eisenbrey, T. Sollmann, W. B. MacNider, H. P. Sawyer, J. A. Sampson, etc.

The attempts to produce pure tubular lesions by means of epithelial poisons (uranium nitrate, the chromates, corrosive sublimate)

³ Archives of Internal Medicine, 1910, v, 133-167.

and pure glomerular lesions by means of vascular poisons (arsenic, cantharidin, venom) have in animals been fairly successful. With diphtheria toxin, it is possible to produce an experimental renal disease in which both the glomeruli and the tubules are severely injured. The more recent studies indicate that uranium nitrate, though it injures the tubular epithelium predominantly, injures also, to a certain extent, the glomeruli.

The investigators of experimental renal disease depended at first too much upon the results of histological study as a control. Since the application of functional as well as histological methods to the study, opinions regarding the exact effects of individual poisons upon the kidney are being modified. The observations of Takayasu, particularly, have revealed the fact that there may often be severe disturbances of function of a part of the kidney when there is little or no evidence of histological lesion there.

Especially instructive on the functional side are the observations of Sehlayer and his pupils, working in Romberg's clinic, regarding the vascular reactions of the two main types of experimental renal disease, namely of glomerulonephritis and of tubular injury. This investigator and his associates have studied carefully the reaction of renal bloodvessels to various stimuli, after these different kinds of injury; they have investigated the relations of the particular injuries to the general blood pressure on the one hand, and to diuresis on the other, studies which have been carefully controlled in this country by Pearce.

More or less successful attempts are being made to ascertain the exact points in the normal kidney in which the various constituents of the urinary secretion are put out (water, sodium chloride, nitrogenous substances like urea, uric acid, etc.). *It would appear that each individual substance which comes out in the urine is subject to its own laws of excretion, and that we must be extremely careful not to transfer the findings regarding the excretion of one substance to the excretion of another, even though it may seem to be closely allied, chemically, to the former.* This opens up a large field for experimental work; for each substance will have to be studied in its excretion-relations, under a whole series of experimental pathological conditions, as well as in various clinical states. There is a good deal of evidence, too, that in pathological states, functions ordinarily carried on by certain of the histological constituents, may when they are diseased, or destroyed, be taken up by other histological constituents, which ordinarily are not concerned with them. This "give and take" theory of renal function has been emphasized, especially by J. McCrae.

The view held at present, that renal edema depends upon diminished glomerular permeability on the one hand, and increased permeability of the cutaneous vessels, on the other, has already been referred to.

It marked a great step forward when P. F. Richter, in 1904, showed us how, experimentally, to produce, in animals, a nephritis accompanied by dropsy, thus reviving interest in the important but long overlooked observation of Chittenden and Alexander Lambert, in 1899, of the occurrence of ascites in uranium poisoning, and of Woroschilsky, in 1890, of general edema and dropsy in the same poisoning. With the new experimental method easily available, the questions of the influence of water retention, of salt retention, of renal vascular injury, of cutaneous vascular injury, etc., could be vigorously taken up, and while opinions are not yet fully in accord regarding these various points, there is every reason to believe that investigations are on the right path, and that before long many of the debatable questions will be satisfactorily answered. It seems certain now that in edema there is injury not only to the kidneys, but also to the bloodvessels all over the body. In getting rid of edema, we have to consider both components.

Not the least interesting, on the experimental side, are the researches dealing with the relation of arterial hypertension and cardiac hypertrophy to experimental renal disease. The well established clinical relations have received support, on the experimental side, through the observations, of Paessler and Heineke, bearing upon changes in the blood pressure after experimental reduction of kidney substance in the body, and through the careful studies of Carrel and Janeway in the same direction. These observations show, that when the amount of kidney substance is reduced beyond a certain limit, hypertension results. They do not, however, explain the exact mechanism by which the hypertension arises, and speculation is still rife as to the pathogenesis. The majority assume a toxic influence leading to the hypertension, though some accept the glomerular reflex theory of A. Loeb.

While the loss of large numbers of glomeruli, or injury thereto, results in arterial hypertension, extensive epithelial injury (tubules) without glomerular lesions, seems to result sometimes in hypotension. Interesting in this connection are the observations of R. M. Pearce, who found that the depressor substances normally present in the urine disappear from it after experimental injury to the epithelium of the tubules.⁴

The study of the origin of uremic symptoms, in renal disease, is the part of the subject which has thus far been least advanced by experimental work. While in experimental animals it is sometimes possible to produce gastro-intestinal disturbances with associated respiratory and circulatory symptoms, ending in coma and

⁴ Great difficulty has been encountered in producing, experimentally, a chronic nephritis comparable to chronic nephritis in man. Thus far, the experiments of E. C. Dickson have been most successful in this direction. It is reasonable to assume that it will be easier to produce, experimentally, a chronic glomerulonephritis with secondary contraction than the so-called primary contraction (arteriolar nephropathy).

death, as yet no satisfactory explanation of the origin of these symptoms has been given and experiment has contributed nothing that we did not already know from clinical observation. That this dark corner of renal pathology will later on be lighted up, as the result of experimental inquiry, there can be no reason to doubt.

When progress is making so rapidly in many different directions in experimental renal pathology, great caution must be observed in transferring the results, uncritically, to human pathology. As to the conditions in human beings, the last word must be left to studies in the clinic.

CONCEPTIONS OF RENAL DISEASES BASED ON THE CHEMISTRY OF THE COLLOIDS.

Very recently, an attempt has been made to approach the problems of the nephropathies, both clinically and experimentally, from the starting point of colloid chemistry. The latter is a brand-new science. When the present generation of physicians was in training, the chemistry of the colloids was only making a beginning, but during the last fifteen years, advances in knowledge concerning the colloids have been made with such great rapidity, that text-books, presenting only an epitome of the subject, today, make large volumes.⁵

In the future, a training in the medical sciences must include, besides a knowledge of the physico-chemical laws which govern the crystalloids, a thorough grounding in the principles and facts of colloid chemistry. For the world of biological phenomena is both crystalloidal and colloidal in nature, and colloidal chemistry has the task of doing for living organisms what physical chemistry has done and is doing for the crystalloid world. This is obvious when we recollect that the proteins of the body, as well as its lipoids, and its carbohydrates, making up the cells and the details of their histological structure, and even the blood plasma, are in a colloidal state. Colloidal states of substances are met with sometimes in a liquid form, when they are known as *sols*, sometimes in a solid form, when they are known as *gels*.

Substances in a colloidal state, at least in their typical examples, are "heterogeneous systems," that is to say, they are spatial combinations of coexisting phases (for example, solids with liquids, or liquids with liquids). These phases are so in contact with one another that the surface relations are extremely large, that is,

⁵ Pösch (V.), *Introduction to the Chemistry of Colloids*, English translation by H. H. Hodgson, 1910; also, Zsigmondy's *Colloids and the Ultramicroscope*, (Wiley) 1909; Pauli (W.), *Physical Chemistry in the Service of Medicine*, translated by M. H. Fischer, New York, 1907; Bechhold (H.), *Die Kolloide in Biologie und Medizin*, Dresden, 1912; also Zsigmondy (R.), *Kolloidchemie*, ein Lehrbuch, Leipzig, 1912; Ostwald (Wo.), *Grundriss der Kolloidchemie*, Dresden, 1909; Freundlich (H.), *Capillarchemie und Physiologie*, Leipzig, 1909; Müller (A.), *Allgemeine Chemie der Kolloide*, Leipzig, 1907.

there are an enormous number of scattered particles in a given volume of fluid. Moreover, the phases within the system are so distributed that the whole system gives the impression of being homogeneous. Such heterogeneous systems, with these two peculiarities (great surface development, and external appearance of homogeneity), are known as *dispersoids*. The one phase, consisting of separate particles scattered through the other phase which is a continuous substance, is called the *dispersive phase*, while the continuous substance itself, is called the *medium of dispersion*. The colloidal particles of a dispersive phase vary in size; some of them (the larger ones) are of a size corresponding to the lowest limit of microscopic visibility (0.1 micron), others, (the smaller ones), approach in size the lowest limits of ultra-microscopic visibility (0.001 micron), ultramicroscopic particles being those which are too small to be directly visible, but large enough to scatter, and polarize, a beam of light; the very smallest particles in a colloid state seem to approach in size the larger molecules of crystalloid substances—the transition-area between the colloid and the crystalloid world. When the dispersive phase consists of the larger particles, we have to deal with the so-called “dispersions proper” (including colloidal suspensions and colloidal emulsions), when it consists of smaller particles we have to deal with the so-called “colloidal solutions;” when a dispersive phase consists of particles smaller than 0.001 micron we have to deal no longer with colloid states, but with crystalloid solutions (molecular dispersoids and ionic dispersoids). In colloidal suspensions, the dispersive phase is solid, the medium fluid; in colloidal emulsions both phases are fluid. The same chemical substance may sometimes exist as a suspension-colloid, at others as an emulsion-colloid.

Partly responsible for the peculiar behavior of substances in colloidal state, are the tremendous surface energies which they develop and which have chemical, physical, and electrical importance. In this surface-energy, the capacity-factor is the size of the surface, the intensity-factor is the surface-tension. If one recalls the way the gases oxygen and hydrogen may be concentrated and chemically united on the surface of finely divided platinum, platinum sponge (as contrasted with the minimal influence of an equal weight of solid platinum), it will serve as an example of the effect of surface energy and its transformation through volume energy into chemical energy. Other interesting examples of absorption are seen in the capacity shown by certain colloids to take finely divided substances out of solution and to hold fast to them; such adsorption phenomena appear to be significant in connection with the behavior of lecithin, and of ferments, in the animal body.

Substances in colloidal state (dispersions proper) differ from the molecular dispersoids or crystalloids (like solutions of NaCl, sugar, etc.) in that they do not diffuse on dialysis, because the dispersive

phase consists of particles too large to pass through the pores of parchment paper or animal membrane. They have less Brownian movement and very little velocity of diffusion, and so have only a very slight osmotic pressure, or none at all. The internal friction, or viscosity, varies in different colloidal states; in emulsoids, it may increase rapidly with concentration, or change in temperature so as to pass from a fluid to a jelly.

All colloidal particles in the dispersive phase are electrically charged. Since the electrically charged particles mutually repel one another, the colloids remain in solution or suspension, and if the electrical charge be taken away, precipitation occurs. It is interesting that the electrical charges can be taken away by the addition of electrolytes. Further, on passing an electric current through a colloid, the charged particles, according as they are negatively or positively charged, will wander toward the anode or cathode (cataphoresis).

Life depends upon the existence of substances in colloidal states in the body-cells. In physiological and pathological processes, colloidal states undergo many "changes of condition." Thus sols are often converted into gels, (process of gelatinization). The process, in true gelatinization, is reversible; the gels can again be converted into sols and we may have to deal with alternating gelations and liquefactions. The process of gelatinization is closely allied to the phenomena of "swelling" or "imbibition," that is, to the property possessed by many substances to take on a jelly-like form (or emulsoid state) when placed in contact with fluid.

Now, the amount of water in every cell, the "turgescence of the cell," and the extent to which the cell constituents may pass from a *gel* to a *sol* state, or from *sol* to *gel*, are determined by properties peculiar to colloids. Thus protein substances have a specific avidity for water, varying with the conditions under which the colloid is placed. For example, both acids and alkalis change the avidity for water—increasing it; while salts may either increase, or decrease, the capacity to take up and hold water. It appears that bromides, nitrates, chlorates, and chlorides increase the capacity for swelling, the bromides most, the chlorides least; while acetates, citrates, tartrates, and sulphates decrease the capacity for swelling, the acetates least, the sulphates most.

On account of this important relation of acids and alkalies to the swelling capacity, I desire to call attention to some most important studies made by L. J. Henderson, of Cambridge, Massachusetts. He has tried to detect how it is that the blood is neutral and retains its neutrality against much acid or alkali. Henderson's studies seem to me to be of the greatest importance for the whole doctrine of equilibrium between bases and acids in the animal organism.

The body behaves as though it were very eager to preserve this equilibrium, and, in the preservation, it makes use of two sets of regulatory mechanisms, one internal and one external, which overcome the acidity which metabolic changes tend to produce.

In the internal mechanism, the blood, the tissue cells, and the tissue juices are concerned. Here, there is a chemical regulation, through which neutrality is maintained, largely by means of the phosphates and carbonates ("Henderson's factor"), partly by means of the proteins (acting as amphoteric electrolytes to neutralize either acids or bases, according to need, by dissociating in the one case as bases, in the other as acids.)

In the external mechanism, the functions of various secretory glands are concerned; thus, (1) through the excretion of CO_2 by the lungs, (2) the excretion of acid sodium phosphate, of uric acid, and of CO_2 by the kidneys, and (3) the excretion of acid in the sweat, the body possesses important means for getting rid of an excess of acid.

Now, in pathological states the tissues of an organ, owing to the action of toxins, or to circulatory changes, may conceivably accumulate acid in excess.

In several publications Martin H. Fischer,⁶ of Cincinnati, has boldly pushed forward a conception of nephritis based upon colloid chemistry, on the one hand, and upon a disturbance of the equilibrium between acids and bases in the organism, on the other. He asserts that all the changes that characterize "nephritis" are due to a common cause; namely, to the abnormal production or accumulation of acid in the cells of the kidney. Resulting from this excessive acidity there is abnormal swelling of the tissue structures, which accounts, in his opinion, for the albuminuria, the cloudy swelling, the formation of casts, the quantitative changes in the urine, and the changes in the amounts of dissolved substances excreted. He supports his ideas by experimental work in animals and by clinical observations on human beings.

Applying what has been said above regarding the action of neutral salts upon the swelling capacity, Fischer believes that he has experimentally counteracted the effects of abnormal acidity in the kidney by the action of neutral salts, thus restoring normal structure and function. For example, by injecting HCl , alone, into animals he could produce an acute nephritis, whereas the same amount of HCl , injected along with concentrated solution of sodium chloride, caused no nephritis.

Fischer reports a number of clinical cases, some of them very severe with anuria and coma, and asserts that they made a rapid recovery by treatment with sodium carbonate and sodium chloride given per rectum.

Fischer's views have called forth rather severe criticism from a

⁶ See especially his volume on "Edema," and another on "Nephritis,"
VOL. 145, NO. 1—JANUARY, 1913.

high source,⁷ partly, it would seem, on account of the dogmatic way in which the views have been presented, and his neglect adequately to value studies of the nephropathies made by other methods.

Personally, I am very much interested in Fischer's conceptions, though perhaps more in the starting point of his experiments than in any goal thus far reached. I think he may be doing a very real service in emphasizing the importance of studies in physical and colloid chemistry for the further investigation of normal and pathological renal phenomena, and I hope that experimenters trained in physical and colloid chemistry may coöperate actively with other investigators, trained in the methods of renal investigation hitherto used, to extend our knowledge of renal function and renal disease.

I may say that some (as yet unpublished) studies of Dr. A. W. Sellards, who is in charge of the chemical division of the laboratory in the clinic in which I work, indicate that, in a certain proportion of nephropathic patients, a very much larger amount of sodium bicarbonate has to be injected into the blood to make the urine alkaline than is required in normal individuals; but there are also many nephropathic patients, he finds, who respond by an alkaline urine to quantities of sodium bicarbonate (introduced intravenously), no larger than those required to make the urine alkaline in normal individuals.

It is interesting to note that von Hoesslin⁸ found that the administration of sodium bicarbonate in rather concentrated solution led to a decrease in the albuminuria, in cases of renal disease studied by him; and it may be worth pointing out that Straub and Schlager⁹ have shown that the carbon-dioxide tension of the blood may stand in relation to the amount of albumin excreted by the kidneys, at least in certain forms of albuminuria.

ON CERTAIN FUNCTIONAL TESTS APPLIED TO THE KIDNEYS.

Through the researches of Albarran, Israel, Caspar and Richter and von Koranyi, various methods of testing the functional efficiency of one or both kidneys have been worked out. Some of these methods have been helpful, especially in the determination, in unilateral renal disease requiring nephrectomy, of the functional efficiency of the kidney on the other side, the urine being collected separately, by ureteral catheterization.

The phenolsulphonephthalein test, introduced by Rowntree and Geraghty,¹⁰ is the most important recent addition to our methods

⁷ Archives of Internal Medicine, 1912.

⁸ Deutsch. Arch. f. klin. Med., cv, 147.

⁹ Münch. med. Woch., 1912.

¹⁰ Archives of Internal Medicine, 1912, ix.

for measuring the functional efficiency of one, or both of the kidneys. To insure free secretion, the patient is given from 200 to 400 c.c. of water, twenty or thirty minutes before making the test. The bladder is emptied by aseptic catheter, the exact time noted, and 1 c.c. of the test solution ($= 0.006$ gram of the chemical) is injected intramuscularly, in the lumbar region. The urine, as it drops out of the catheter, is collected in a test-tube containing a drop of NaOH solution (25 per cent.), until a faint pinkish tinge appears (time noted). The catheter may then be withdrawn, and the patient voids at the end of one hour, and again at the end of two hours, each voiding being separately collected. The amount of phenol-sulphonephthalein in each is quantitatively determined by means of a colorimeter, after taking the specific gravity, rendering the specimen alkaline with NaOH, and diluting it to one liter with distilled water. With Rowntree and Geraghty's modification of the Autonrieth-Königsberger colorimeter, the percentage can be read off at once, by noting the position of the indicator on the scale.

Normal individuals excrete from 50 per cent. to 65 per cent. (average 57.5 per cent.), in the first hour. When renal efficiency is impaired, the output may be, quantitatively, greatly decreased, and the excretion is delayed.

The test can be used, either to estimate the total excreting function, in bilateral renal disease, or for a comparison of the efficiency of the right kidney with that of the left, in unilateral disease. In the medical and genito-urinary clinics at the Johns Hopkins Hospital, Drs. Rowntree and Geraghty have made many tests which establish the clinical value of the method. During the last year Dr. Helen Watson has applied the test, in the medical clinic, in over 100 cases, with confirmatory results, and, at the suggestion of my colleague, Dr. Thayer, Drs. Rowntree and Fitz have carefully compared the findings after the phenolsulphonephthalein test, in a series of cases, with those after Schlayer's tests, (KI, lactose, and NaCl).

Schlayer and Takayasu, of Romberg's clinic, are of the opinion, as a result of their experimental and clinical work, that NaCl and KI are excreted by the epithelium of the renal tubules, and that lactose and water are excreted by the glomeruli. In experimental nephropathies (1909), they found that destruction of the tubular epithelium resulted in impaired excretion of NaCl and of KI; the greater the injury, the worse was the excretion. In these cases, the renal bloodvessels, they assert, were uninjured, and water and lactose were excreted in much the same way as by the normal kidney. In the animals in which the renal vessels (glomeruli) were injured, the excretion of lactose was found, by them, to be delayed.

They then applied these tests to human beings, not to determine the sufficiency or insufficiency of the kidneys (as regards their

eliminating power for the total needs of the body), but rather for the purpose of gaining an insight into the mode of working of diseased kidneys, and to ascertain what changes in the functions of tubules, or vessels, have occurred in a given patient.

In making the *lactose test*, 20 grams of milk sugar dissolved in 20 c.c. of distilled water, the solution having been previously Pasteurized at 75 to 80° for four hours on each of three successive days, are injected into a vein at the bend of the elbow; the urine is collected at hourly, or half-hourly, intervals, and tested with Nylander's solution until the reaction for sugar ceases to be positive. The excretion may be followed quantitatively if desired by polarimetry. Normally, all the lactose is excreted in four or five hours. In many cases of renal disease, the excretion is not completed in seven, nine, twelve, or more hours. The authors assert that, *in such cases of delayed lactose excretion, the renal bloodvessels are diseased.*

In making the *potassium iodide test*, 0.5 gram is given by mouth, and the urine tested every two hours for KI (Sandow's method). Normally, excretion is complete in from 30 to 55 hours. In certain renal diseases, the excretion is prolonged beyond 60 hours, and the authors assert that, *in such cases of delayed KI-excretion, the renal tubules are diseased.*

To determine the presence or absence of an hyposthenuria, and, if present, its type (tubular or vascular), the intake and output of water and of sodium chloride are carefully followed, in the functional testing of Schlayer and Takayasu. They believe that their methods suffice, clinically, to differentiate nephropathies with predominantly tubular lesions from those with predominantly vascular lesions. Thus each nephropathic case is, according to them, to be studied in two directions: (1) as to how KI is excreted (tubular function) and how lactose is excreted (vascular function), and (2) as to how H₂O and NaCl are excreted; if an hyposthenuria be found to exist, one ascertains whether the specific gravity of the hyposthenuric urine is very low (tubular nephropathy), or relatively high (vascular nephropathy), and also if the capacity to eliminate an increased intake of NaCl is lost (tubular disease), or still retained (vascular disease).

The application of these methods is not quite so simple as it sounds, or, rather, considerable caution has to be exercised in interpreting results, owing to certain extrarenal factors which must always be kept in mind. The studies made by Rowntree and his associates indicate that the phenolsulphonephthalein test is a much more reliable indicator of tubular function than the KI test. Schlayer's lactose test may prove to be of very great value.

These studies are all in the right direction, and there is every prospect that functional testing of the kidneys will steadily grow in clinical importance.

SOME THERAPEUTIC PRINCIPLES BASED ON OUR PRESENT KNOWLEDGE OF RENAL DISEASE.

Here, first of all, let me speak of *prophylaxis*. In the nephropathies, perhaps, more than in diseases of other parts of the body, it is easier to ward off a malady than, once it is established, to cure it. What I have said regarding the etiology of the nephropathies gives the clue to the prophylactic measures at our disposal.

To prevent the ascending (urinogenous) nephropathies we try to prevent (1) all obstructions to urinary outflow, and (2) all infections of the urinary passages. When an infection of the lower urinary passages exists, we may try to prevent an ascent (1) by proper treatment of the primary infection, and (2) by copious water-drinking, and the use of hexamethylenamin. In women, some of the infections of the bladder and of the pelvis of the kidney with *bacillus coli communis* may be due to chronic constipation.

To prevent the descending (hematogenous) nephropathies, we have to learn how toxemias and bacteriemias may be avoided.

Thus, the prophylactic measures to be taken against the toxic tubular nephropathies (sublimate-kidney, chromate-kidney, phosphorus-kidney, etc.) are obvious. How to prevent the pregnancy-nephropathy in the people who are prone to it, we do not yet know, but the knowledge that it is due to absorption from the cavity of the uterus, and that emptying the uterus, in the majority of cases, cures it, stands us in good stead. And since the toxic glomerular nephropathies—the true glomerular nephritides—are often due to streptococcus toxines, the possibility of the complication should be thought of in every case of streptococcus infection. It arises most often after streptococcus sore throat. Here the general practitioner can do much in the way of prevention. *Every individual who suffers from sore throat, tonsillitis, or a "bad cold" with fever, should be put to bed, and be kept warm there, until the infection is overcome.* Not only would much renal disease be thus avoided, but also many serious diseases of the heart and of the joints. If infections of the tonsils keep recurring, the risk to the kidneys, endocardium, and joints is very great; in many cases, it may be wise completely to excise the infected tonsils. Other foci of chronic infection should be watched for, and, if found, removed (sinusitis; pyorrhea alveolaris; abscesses of the roots of teeth, otitis media; chronic appendicitis; chronic cholecystitis; chronic prostatitis; chronic salpingitis, etc.).

After scarlet fever, patients should be kept in bed for at least four weeks after the onset of the disease, and from the middle of the second week on, the body should be kept warm, and only warm baths should be given, the patient's diet consisting of milk and cereals.

The focal nephropathies, due to bacteriemias, could doubtless often be avoided by preventing, or properly treating, the primary infection preceding a bacteremia. But we have far to go before we shall learn how to do this in all cases.

Most important at present, perhaps, are our attempts to prevent what I have designated as the arteriolar nephropathy, or genuine contracted kidney due to atherosclerosis of the small arterioles. Prophylaxis here should be directed toward the conditions (toxic) which give rise to the premature atherosclerosis of the arterioles of the organs. Particularly in families in which there is a history of the disease in one, or several, of its members, precautions should be taken early. Over-indulgence in food, especially protein food, in alcohol, in tobacco, and in the pleasures of sex and work may be warned against; if arterial hypertension have already appeared, a strict regime should be instituted and maintained.

In the *treatment* of renal diseases, the dictum of Traube still holds good: "Protect the kidneys and control the heart." In addition to the principle of protection, we can also, at certain stages, successfully apply the principle of exertion to the renal function.

In the protective therapy, we avoid, as far as possible, all further injury to the kidney by intoxication (lead, gout, alcohol, etc.), or infections (chronic tonsillitis, anginas, etc.), and we can lessen, also, the amount of work thrown on the kidney, in normal metabolism, (1) by choosing a suitable diet (limitation of proteins to 100 to 125 grams meat, or its equivalent, of water, to 2 liters, of sodium chloride to 8 to 10 grams and irritating condiments; (2) to a slight extent, by increasing the eliminatory functions of other organs (skin, intestines, lungs); and (3) by lessening the amount of physical or mental work done each day and advising periods of rest, lying down, in the middle of the day. In cases in which the renal disease is compensated, such protective measures are all that is necessary.

To get patients well started on a suitable dietetic regime, the foods should at first be carefully weighed or measured. For this purpose, Dr. C. W. McElfresh, of Baltimore, has found it very helpful to enlist the aid of nurses especially trained in dietetics.

In every case of renal disease, the condition of the heart should be carefully watched. Indeed, chronic passive congestion of the kidneys, due to cardiac insufficiency, may, of itself, cause marked albuminuria and cylindruria. The albumin, as well as the casts, may disappear from the urine when cardiac compensation is reestablished. And when the kidneys, themselves, are diseased, the urinary symptoms may be markedly exaggerated if the heart begin to fail. "Every renal patient is also a cardiac patient;" in treatment, this should always be kept in mind.

The treatment of cardiac insufficiency, I shall not go into at this

time, as I have already dealt with that topic in a former paper.¹¹ When the renal disease is not compensated, the kidneys having become insufficient, the rest of the body begins to show certain ill effects, of which the two most important are (1) edema and (2) uremia. In such cases we must make our protective regime still more rigorous, often keeping the patient in bed at complete rest for a time; in addition, we may find it necessary to stimulate renal excretion by diuretics which improve the blood flow through the kidney and excite the renal epithelial cells to increased work.

In combating edema in renal disease, we use diuretics, a salt-poor diet, mild purgatives, and when necessary heart tonics. Diuretin, and the still more powerful theocin, are both excellent stimulants to the renal epithelium, while digitalis preparations improve the circulation in the kidney. In giving diuretin, a dosage of 0.5 gram at 2 P.M. and the same amount at 5 P.M. every other day for a few days may suffice; if not, as much as 4 grams may be given in one day. In giving theocin, 0.1 to 0.2 gram at 10 A.M. and at 4 P.M., every other day for a few days may suffice; if not, as much as 0.8 to 1.0 gram may be given in twenty-four hours. The renal cells may cease to respond; if so, the medication should be stopped, to be tried again a few days later.

Mild purgation is usually sufficient. Violent purgation is often harmful, exhausting the strength of the patient.

The influence of a salt-free (or salt-poor) diet, in reducing renal edema, is sometimes remarkable, especially in acute cases; but a salt-free diet should never be kept up for a long time, or it will do more harm than good. The intake of NaCl may be reduced to 2 or 3 grams per day; in many instances, a reduction to 5 grams per day may suffice. The patient is told to add no salt to his food, and he may use salt-free bread and unsalted butter, together with one liter or one and a half liters of milk.¹² Sugar, rice, potatoes, stewed fruit, fresh green vegetables, salad, chocolate, coffee, tea, and cereals, if no salt be used in their preparation, are practically salt-free foods. Meat and eggs are also salt-free, but should not be used to any great extent, in such cases, on account of their high protein content. In the French clinic of Widal, a salt-poor diet consisting of 200 grams of salt-free bread, 200 grams meat, 250 grams vegetable, 50 grams unsalted butter, and 40 grams sugar is employed. Such a diet contains 1500 calories, and is sufficient for a patient lying in bed. It represents about 60 grams of protein—a low value. I have seen patients, on a similar diet, lose 20 to 30 pounds in a week, from reduction of the edema. The strict salt-free (or salt-poor) diet should not be continued longer than a week at a

¹¹ On the Treatment of Some of the Forms of Cardiac Failure, Virginia Medical Semi-Monthly, 1911, xv, 457 to 486.

¹² Milk is not salt-free; it contains 1.6 grams of sodium chloride per liter.

time, preferably not over three or four days; then a little more salt (1 to 3 grams) may be permitted, but as far as possible the individual tolerance should be determined, and the patient kept within it. When the patients have a high tolerance for NaCl, there is no good in restricting the salt intake to very small amounts.

In the treatment of uremic symptoms, similar principles are followed, namely, vicarious elimination by mild purgation and diuresis, cardiac tonics, protective diet. When uremia is threatened, it may be well to limit the food, for a short time, to milk sugar, dissolved in water, and fruit juices; later milk may be added. In some cases of uremia, venesection may be life saving; when convulsions recur frequently, lumbar puncture may be tried. In uremic asthma, a small dose of morphine may be necessary. If there be insomnia, or marked nervousness, we may give 0.1 gram of veronal at 2 P.M., at 5 P.M., and at 8 P.M., for a time.

In the management of contracted kidney, we attempt to prevent further action of the cause (atherosclerosis; streptococcus intoxications). To combat a developing atherosclerosis, the whole mode of life has to be systematically ordered. A lacto-vegetarian regime is instituted, and several small meals per day substituted for three large ones. Constipation, if present, is overcome, as is also abnormal intestinal fermentation (administration of *Bacillus bulgaricus*). The blood pressure should be watched, but it must be borne in mind that the hypertension is a compensatory process, rarely to be combated directly by the high frequency current or by vasodilating drugs (nitroglycerin; sodium nitrite; vasotonin), but, as far as possible, by a prevention of the intoxication which causes it, that is to say, by dietetic and general hygienic measures. Above all, the strength of the heart must be maintained, for unless he die from an apoplexy, the patient suffering from contracted kidney, sooner or later, suffers from cardiac insufficiency. When this begins to appear (dyspnea; cardiac edema), or if uremia be threatened, complete rest and digitalis therapy are indicated; diuresis may be favored by diuretin or theocin, the bowels kept open by mild laxatives, and the skin active by warm packs. Violent sweating is to be avoided.

In contracted kidney, the patients usually pass large quantities of urine. Sudden reduction of the amount is usually a bad sign; it may indicate either a failing heart, or an acute nephropathy, superimposed upon the contracted kidney.

If his life be well regulated, a patient suffering from contraction of the kidneys may go along for many years, even for decades, in comparative comfort, especially if he choose a good climate to live in and avoid infections and chilling of the skin.

THE INFLUENCE OF EXERCISE ON THE HEART.¹

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THE hour has arrived for a complete reconsideration of the whole question of exercise in relation to the heart.

The invention of new instruments of precision has been followed by the compiling of statistics obtained from observations on the blood pressure, pulse rate, and heart sounds, in normal young people at rest and under exercise; and the frequency of enlargements, variations, and irregularities has been demonstrated, transient or functional in character for the most part, but which might with propriety be termed variations within the normal rather than evidences of a pathological state.

Much medical opinion has of necessity been founded on the evidence of single or occasional cases, or even on that last refuge of the indefinite, "years of experience," which with so many men takes the place of accurate observation, and in consequence children have been classed as diseased or defective and ruthlessly forbidden the exercise and play essential to their physical welfare both present and future. James Mackenzie wisely says, "I have seen numbers of these going through elaborate methods whom I would have sent out to the play fields."

The mere presence of a heart murmur has been considered so serious and disabling in character that the necessary activity of many young people has been harmfully curtailed. Its importance in the field of cardiac symptoms has been grossly exaggerated and too often the more grave and significant signs of heart weakness have been put too far into the background.

As the result of a conversation with Professor Wenckebach, formerly of Groningen now of Strassburg, in which he deplored the lack of accurate information as to the frequency of heart murmurs in different postures of the body and under conditions of rest and exercise in the normal youth, the following observations were taken at the University of Pennsylvania on the incoming class of students whose ages lay between seventeen and twenty-five years:

In common with all well-regulated schools and colleges in America, this university requires a thorough medical examination from all its students on entrance before beginning the course in physical education, which is an integral part of their college work. Out of the thousand and more who came up for this examination in October

¹ Read before the section on Physiology of Exercise, XV International Congress of Hygiene and Demography, Washington, D. C., September 29, 1912.

only those were chosen who presented no apparent defect during the regular medical test. These selected men were given a more careful and thorough heart examination, and when any doubt was felt about the presence of a murmur, two and sometimes three observers made separate examinations.

The selected student took fifty steps of stationary running, raising the knees high at each step so that the heart was brought to a state of great activity. He then lay down on a couch, then sat on a chair, and finally stood up, the stethoscope being applied in each position. For conducting the work and tabulating the results, I am glad to acknowledge with thanks the invaluable assistance of Dr. Ira Ayer. The report includes murmurs only. There were a few cases of arrhythmia or accented aortic or pulmonary second sound without murmur, but these have not been included; nor has note been made of any general conditions like anemia. Such cases were few and the reporter wished to confine himself within the limits of his subject, namely, the frequency with which murmurs develop upon light exercise in individuals in whom no heart lesion is known to exist.

Murmurs that were doubtful have been included, and a few very faint ones that were evanescent were placed in that category. They have been classified according to location under six heads, as follows: (1) apex, (2) apex and base, (3) fourth space just left of sternum, (4) pulmonic, (5) aortic, (6) aortic and pulmonic. They have been classified according to intensity into very faint, faint, moderate, and loud. The quality was in almost every case soft and blowing and puffing, although in a few cases the tone was slightly harsh.

Murmurs were found in 74 out of the 266 men examined (27.8 per cent.), of these 35 were of the pure pulmonic systolic type, and if we include those in which it occurs in combination with others it was present in 64 cases, only 10 men out of 74 failing to show it.

Murmurs were much more frequent in the recumbent position. When they were audible in all three postures they were accentuated when the patient lay down and as the pulse became slower and stronger. This is not to be accounted for by the rotation in which the examinations were made because the order was changed and reexaminations were frequently made to confirm their result. The following is the table of results:

TABLE OF MURMURS FOUND IN APPARENTLY NORMAL HEALTH AFTER
 EXERCISE—FIFTY STEPS, STATIONARY, RUNNING.

E = evanescent. B = observed before exercise. V = variable. U = unclassified in strength.

		V. Ft.	Ft.	Mod.	Loud.	Before.	Unclassified.	Total.
Apex	Lying	1, E.	1, B.	1, B.		
	Standing	1, E.	1, B.		
	Sitting	1	1	2	7
	L. S. S.	1	1	2	7
Apex and base	Lying	1, E.	1, B.		
	Standing	1, E.	1, B.		
	Sitting	1	1	3	8	
	L. S. S.	1	1	3	8	
Fourth space left of sternum	Lying . . .	2	31, E.	2	1	1, V.	
	Standing	1	1, V.	
	Sitting . . .	1	3	2	1, E.	18
	L. S. S. . .	1	3	2	1, E.	18
Pulmonic	Lying . . .	1	41, E.	31, E.	2		
	Standing . . .	2, E.	2		
	Sitting . . .	1	5	3	1, E.	9	35
	L. S. S. . .	1	5	3	1, E.	9	35
Aortic	Lying	1	1	2
	Standing	1	1	2
	Sitting	1	1	2
	L. S. S.	1	1	2
Aortic and pulmonic	Lying	1	1		
	Standing	1		
	Sitting	1		
	L. S. S.	1	3

No marked difference could be found between men who had led an active athletic life and those whose occupation had been sedentary, although murmurs seemed rather to haunt those of inactive habits rather than the more vigorous and athletic. The presence of murmurs in nearly 28 per cent. of normal young men even on slight exertion should, however, lead to caution in giving an unfavorable prognosis when they are found immediately following severe strain or fatigue.

The appearance and disappearance of murmurs by change of posture alone is significant of their unreliability to determine the presence of a real heart lesion when other symptoms are absent.

I have purposely given this investigation in detail because it shows clearly one frequent variation within the normal, and illustrates the fallacy of diagnosing heart damage from the presence of a murmur only.

Athletic exercise may be divided for our purpose into movements in which a maximum effort or short series of efforts predominate, such as shot-putting, weight-lifting, heavy gymnastics, and sprinting; and movements of endurance in which the single effort is slight but the series prolonged to exhaustion, like walking, cross-country running, cycling.

Exercises of effort produce a sudden and rapid rise in blood pressure to 200 mm. and more, which rapidly falls when the effort is over, the pulse returning quickly to its normal rate. The resili-

ency of the heart and arterial system is tested by such exercises, and they should be avoided by those of advancing years.

Exercises of endurance show a slower rise in pulse rate, and the blood pressure never rises to a great height; but even after the pulse has returned to its normal rate the pressure remains high, returning slowly to the normal. Exhausting tests of endurance, such as take place in long races, are in consequence not adapted to the best development of young and growing children, because of the long-continued period of high blood pressure which they entail. Sudden rise and fall found in exercises of effort have but a minor effect on the elastic vessels of youth.

These two forms of exercise are combined to a high degree in boat-racing. In a four-mile race a series of maximum efforts is continued for twenty minutes; the pulse increases its speed, and the blood pressure rises. The first feeling of exhilaration is replaced by discomfort, followed rapidly by a sense of constriction and pain in the chest and head, anxiety, breathlessness, mental confusion, and in extreme cases by fainting. The oarsman fights desperately for breath, the heart dilates widely as a matter of economy, because every muscle can work better when slightly stretched. This dilatation remains until the equilibrium is reestablished in the circulation and respiration.

Murmurs always appear and slowly fade away; after the most severe strain one can seldom find any measurable injury in a week's time in a heart originally sound if the athlete has not passed thirty; occasionally, however, they persist longer.

It is in those unprepared for violent exercise, and especially when approaching middle life, that the danger of heart-strain is most imminent.

An ex-football player out of condition suddenly tries to repeat the exploits of his former days; sometimes with alarming results. One, a physician, after such an attempt, writes me as follows: "As we finished I became conscious of a sensation of extreme vertigo in addition to the breathlessness which I had hitherto tried to disregard, and sat down just in time it seemed to prevent falling. The chest appeared full to the bursting point, breathing entirely inadequate, and respiration very rapid. I remember feeling my pulse at the onset of the vertigo and finding it almost indistinguishable. The heart beats soon became strong and almost painful in their intensity, but breathing remained difficult for perhaps half an hour. I sat still for that length of time before I felt equal to walking to the dressing-room, and even then my legs were weak and unsteady. I had marked nausea, but did not vomit. There was a little bloody tinge to the scanty sputa, and several people remarked my pallor. I was uncomfortable and shaky all that evening, but after a night's rest I felt as well as ever, and have so continued."

This is undoubtedly an acute dilatation of a heart on which strain has been put in the unfounded expectation that the resiliency of twenty will be found fifteen years later.

Sometimes an elderly man fresh from his office goes mountain-climbing, and at the end of a hard climb finds himself in such distress as has just been described—a distress which does not disappear when he rests. His heart is found badly dilated and recovery is slow, if it ever takes place completely. Only too often the dilatation remains or recurs on the slightest exertion, and he remains a partial or complete invalid for the rest of his life. Cases are on record of rupture of valves in men aged over forty years, but I have found no record of such a case in the young.

If kept within the limits of overstrain and exhaustion systematic graduated exercise is perhaps the best method of building up the heart in size and strength, and even in most damaged hearts there is no better way of keeping up the tone and efficiency than by movements kept within the limit of fatigue. Stokes pointed this out in Dublin, Oertel in Munich, and it has been confirmed by many others. Controversy has raged fiercely, however, over the remote effects of the more active and violent exercises and sports, and too often opinion, prejudice for or against, or vague impression has taken the place of the observation of facts.

The only statistics on which reliance can be placed show the following results:

E. H. Morgan in his report on 294 old oarsmen found an increase of two years in their expectation of life over the selected lives of Farr's English Life Tables.

George L. Meylan in his report on 152 Harvard oarsmen found an increase of 1.6 years, but his results were interfered with by 8 deaths in battle during the Civil War. Allowing them their allotted span, the expectation would show an increase of 5.39 over the selected lives of actuarial tables.

W. G. Anderson found that the graduates of Yale who had won their "Y" on athletic teams showed a mortality considerably less than that of all other graduates.

Dr. Armstrong, of Wellington College, in 198 cross-country and steeplechase runners finds of the 13 deaths from 1870 to 1904 that none died from heart conditions.

Hammett in his exhaustive compilation of distance runners found similar results.

Blake and Larabee, in speaking of Marathon runners, after that most exhausting of all athletic tests, write: "So far as observed no permanent injury of any kind has resulted from participation in these races."

Baruch and Savage, in their most exhaustive and painstaking observation on Marathon runners, come to much the same conclusion, although with more reservation.

It may be taken as demonstrated, then, that even severe athletic competition does not, as a rule, appreciably damage the circulatory apparatus, and its role in hastening the onset of arteriosclerosis is still difficult to determine. Certainly it is not to athletics, but to the much more strenuous occupations continued throughout long hours and under unsanitary conditions, as coal-mining and iron-working, that one must look for information on this subject.

The exhaustion of continual overstrain in the young and growing would of necessity be unfavorable to the child's best interest, but even in them the recovery is so rapid and complete that one is astonished at its thoroughness.

The body is constructed for a life of physical activity and the heart needs constant and varied movement for its proper development. Anything which curtails or prevents this natural means of growth must result in preventing the individual from reaching his highest possibilities.

OBSERVATIONS ON A CASE OF MEDIASTINOPERICARDITIS TREATED BY CARDIOLYSIS (BRAUER).

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HISTORY: J. F., aged twenty-nine years, consulted one of us February 5, 1912. He is single and is a florist by occupation. Formerly he was a steady drinker but during the last two years he has drunk almost none. It is to be noted that the *only illness he has suffered during his entire life was diphtheria followed by "paralysis" at eleven.* The family history is negative.

The present illness began gradually three years ago with "bloating," with tiring easily, and with shortness of breath on exertion. His condition grew rapidly worse and almost from the beginning he has been entirely incapacitated. He says he cannot lie down without several pillows and he spends his nights largely in a chair; he cannot move about without choking and coughing; he is able to eat but little and his abdomen is bloated so that he cannot button his trousers; his bowels will not move without medicine; his urine is scanty and highly colored; he has had much yellowish sputum in which there has occasionally been considerable amounts of blood.

Status Præsens: The patient is a well-developed young man.

Dyspnea and orthopnea are marked. His face is a dusky red, the veins of his neck and face are turgid and a marked venous diastolic collapse is present. In the precordium a violent pulsation is to be seen which consists of a distinct rather slow systolic retraction with a rapid vibratory diastolic thrust. There is a systolic retraction of the left costal arch. Broadbent's sign is present. The respiration is rapid and upper thoracic in type. A marked diastolic shock can be palpated. The apex lies in the sixth interspace in the anterior axillary line. Cardiac dullness extends 3 cm. to the right of the sternum, and to the left as far as the anterior axillary line in the sixth interspace. The area of heart dullness does not change with change of position. Auscultation reveals a loud systolic murmur heard over the entire precordium; this murmur is best heard at the apex. All of the sounds are blurred, the heart action is rapid (120 per minute) and irregular. A second diastolic heart sound can be heard over the entire right ventricle.

There is an obliteration of the left lower pleural cavity. The lower border of the left lung in the precordium does not move with respiration. The right cavity contains a moderate amount of fluid.

The abdomen is much distended. The liver extends a hand's breadth below the costal arch in the nipple line; it is tender and pulsates. Ascites is present. The scrotum, thighs, legs, and feet are moderately edematous.

The urine is highly colored and sharply acid, the sp. gr. is 1030. Albumin and the aldehyde reaction are present; sugar is absent. Hyaline and granular casts and red blood cells are numerous.

The patient was placed in the hospital, where in the course of three weeks, compensation was restored; the heart action became regular, the murmur entirely disappeared, and the heart sounds became clear. The patient's temperature was normal during the entire time.

Ten days later (March 13, 1912) cardiolysis was performed by Dr. J. E. Summers. The purpose of the operation was not only to untether the heart by doing away with the costopericardial adhesions, but also to give the enlarged organ room for freer play.

A U-shaped incision, commencing four inches from the sternum, was made, with its base directed toward the left shoulder, the upper limb skirting the lower border of the second rib as far as the sternum, thence the curved portion overlapping the left border of the sternum to the cartilage of the sixth rib, the lower limb continuing downward, outward, and then upward to the anterior axillary line (Fig. 1). A musculocutaneous flap down to the ribs was raised, and the third, fourth, fifth, and sixth ribs and their cartilages covered by their periosteum and perichondrium were resected flush with the sternum. This exposed the pericardium

and left pleura in an area measuring from above down, five inches: from within, out, four and one-half inches.

The pericardium was found adherent to the chest wall and the pleura somewhat thickened and adherent. It was not necessary to ligate the internal mammary artery, as the costal cartilages were first divided externally to the course of this vessel and then the inner stumps were removed. The wound was closed with a cigarette drain in its lower inner angle, which was taken out at the end of twenty-four hours. The operation was followed by a mild bronchopneumonia, from which the patient's compensation was little disturbed. In other respects convalescence was uneventful.



FIG. 1.—Photograph taken three months after operation, showing incision. The blurring at the apex indicates the freedom of the movement of the heart. (Time exposure.)

The following interesting etiological and pathogenic feature was to be noted in our case. The onset was insidious, and except for diphtheria, when aged eleven years, there had been no definite infection or illness to which the condition could be attributed. The beginning of symptoms in early manhood, at that period in which the chest wall "stiffens," argued that the adherent pericarditis had come down from childhood. As costochondral ossifica-

tion advanced during adolescence, there was an ever-increasing demand for power to mobilize the precordium. The obliteration of the left pleural cavity was significant of a synchronous pleurisy. A chronic adhesive pleurisy, as is well known, becomes a factor of no little importance in a circulatory problem, in which the work to be done approximates the power available. The effect is on the right ventricle, which is always most at a mechanical disadvantage in mediastinopericarditis. The clinical picture pointed chiefly to interference with the action of the right ventricle, and it was clear that in such a condition much was to be expected from cardiolysis.

At Brauer's¹ instigation the first operation for adhesive mediastinopericarditis was performed by Peterson in 1902. Brauer termed the operation cardiolysis, because it loosened the heart from its harness. Since then the operation has been performed some thirty times, with results which depended to a large extent upon the judgment with which the cases were selected. P. Lecène,² from his analysis of 20 cases, states: "The operative mortality of this intervention has been nothing to date. And truly one should not be surprised at this, since on the whole it is only a question of a small operation of general surgery. The anesthesia alone could be dangerous; it is sufficient to watch the anesthetic carefully and reduce it to the minimum." This Gallic surgical optimism is not to be taken too seriously. The dangers of the procedure should not be minimized. Operative mortality should be held to include cardiac deaths occurring in the first days following operation; more deaths have probably occurred than have been recorded.

Brauer postulated that for the success of the operation the following conditions must be present: *diastolic shock, systolic retraction at the apex, and the ability of the heart muscle to compensate*. If from myofibrosis, myocardial degeneration, or from valvular disease the heart is unable to compensate, the operation will be futile. Today we must consider also as generally contraindicated those cases in which the pericarditis is part of a tuberculosis; all such cases in which operative interference has been tried have been benefited little. If the pericarditis is part of a general polyserositis, the results will be bad. Schlayer³ justly maintains that the results of cardiolysis do not depend alone on the condition of the heart. Attention must be given to the serous membranes. In 10 out of 12 cases of his series one and frequently both pleuræ were involved. He believes that the pleuræ in mediastinopericarditis show an extraordinary tendency toward inflammatory processes, and that the processes are by no means transitory, but make for recurrence in the majority of cases. The ascites present must not be considered to be secondary in all cases to cardiac impairment.

¹ Münch. med. Woch., 1902, xlix, 982; Arch. f. klin. Chir., 1903, lxxi, 258.

² Arch. des Maladies du cœur, de Vaisseaux et du Sang.

³ Ueber adhäsive Pericard-obliteration u. Kardiolyse, Münch. med. Woch., 1910, lvii, 729.

If the ascites disappears, with the restoration of compensation, it is probably of cardiac origin; if it does not, it is dependent on a co-existent inflammatory condition of the peritoneum. Schlayer considers two types of mediastinopericarditis: the cardiac and the polyserositic. Anatomically, and to a lesser extent clinically pericarditis may be divided into the following types: diaphragmatic, pleural, chondrocostal, and mediastinopericarditic. The cases may be said almost never to be of a pure type. The existence of the chondrocostal type is necessary if we are to expect anything from operative interference. The heart is hitched fore and aft to the chest wall and to the vertebral column by involvement of the pleura, pericardium, and posterior mediastinum. It is at this double pull that our therapy is directed. An additional indication for rib removal in cardiac disease has been advanced by Alexander Morrison.⁴ In a patient with cor bovinum from mitral and aortic disease who suffered from frequent and severe "anginoid" pains that resisted treatment, he removed $4\frac{1}{2}$ inches and $5\frac{1}{2}$ inches of the fifth and sixth ribs respectively. The result was subjectively and objectively gratifying, so that the patient was able to earn his living, which he had previously been unable to do. He was reported much improved one and one-half years after the operation. Morrison's reasoning was as follows: Experiments show that direct muscle stimulation of the eviscerated heart induces contraction. (One of us has been able to induce contraction in the exposed heart of a five-months-old fetus, four hours after birth, by lightly tapping the right ventricle with a thumb forceps.) The constant thumping of the heart against the stiff and confining chest wall gives rise to a cardiac erythmism. Morrison believes that one of the causes of pain and increased irritability in greatly hypertrophied hearts is this impact of the forcefully beating heart on the chest wall. The substitution of a soft tissue covering for the heart instead of a bony wall admits of free action of the hypertrophied heart without the constant hammering of the chest wall. The free play afforded the greatly hypertrophied and dilated heart by the operation was noticeable in our case. The correctness of Morrison's reasoning must be determined by extensive clinical application of this theory. We would suggest the term *cardiac decompression* in place of thoracostomy, as used by Morrison, because it better describes the purport of the operation.

Tracings made from our patient before and after operation show some interesting features:

Sphygmogram (Figs. 2 and 3): Before the operation the radial pulse was of such poor volume that an adequate sphygmogram was difficult to obtain. During inspiration the pulse was more rapid, and showed less volume—the pulsus paradoxus of Kussmaul.

⁴ Lancet, July 4, 1908; November 20, 1909.

This latter condition has not been materially affected by the operation, but the pulse volume has been much improved. (Vide tracings and legends.)

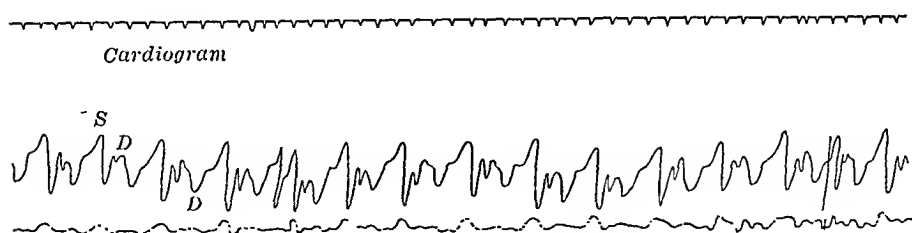


FIG. 2.—Tracing taken at the apex and from the radial pulse two days before operation. *S*, systolic wave; *D*, diastolic wave. Note wave in the diastolic phase of the sphygmogram.

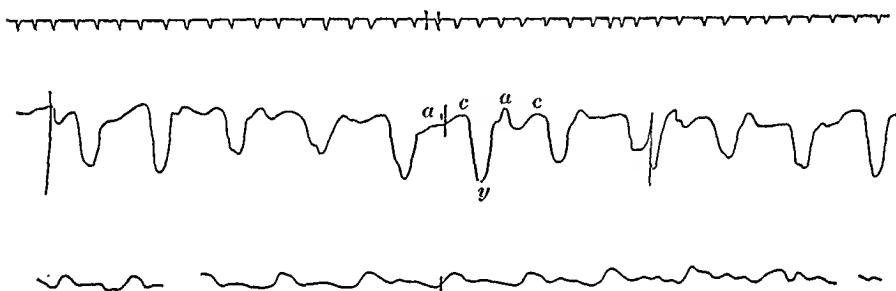


FIG. 3.—Tracing taken from the left jugular vein and from the radial pulse two days before operation. *a*, auricular wave; *c*, carotid wave; *y*, diastolic phase.

Cardiogram: The cardiogram before the operation showed a distinct wave (*D*) in diastole (Fig. 2). This wave was the most marked feature of the cardiogram. Its counterpart can also be seen in the radial tracing; it was synchronous with the diastolic shock. We are at a loss to explain the two wavelets on the crest of the diastolic wave, unless it be a graphic representation of a distinct diastolic vibration, which was palpable, and which was probably due to the resilience of the chest wall. In the systole (*S*) of the cardiogram there is a marked hesitation on the contraction, then completion of the systolic wave followed by a sudden diastolic phase. This feature is not present in the cardiogram taken directly from the apex after the operation. This marked hesitation in the upstroke can be explained by the sudden bringing up of the muscle by the resistance of the surrounding structures which must be mobilized during each systole.

Phlebogram (Fig. 3): The venous pulse taken before operation *after compensation has been restored*, showed a prolonged *a-c* interval and a marked diastolic negative phase (*y*). The shortening of the *a-c* interval and the marked diminution of the diastolic wave (Figs. 4, 5, and 6). After the "untethering" of the right ventricle is a graphic demonstration of the therapeutic value of the opera-

tion. It must be remembered that our control tracing was taken after compensation had been brought about by three weeks in bed and ten days up and about the hospital at comparative rest. Digitalis had not been used for over four weeks before Fig. 3 was taken.

Fig. 4 is from a tracing taken two weeks after the operation. Already the diastolic negative phase is decreased. The tracing of April 9, four weeks after the operation shows still less of the negative phase y (Fig. 5). The phlebogram taken April 22, about six weeks after the operation, shows a normal phase y (Fig. 6).

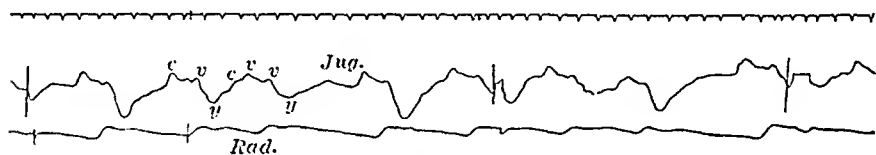


FIG. 4

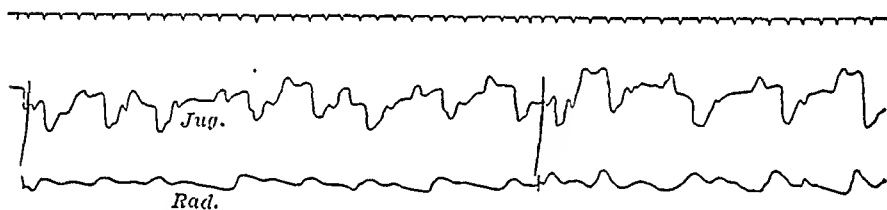


FIG. 5

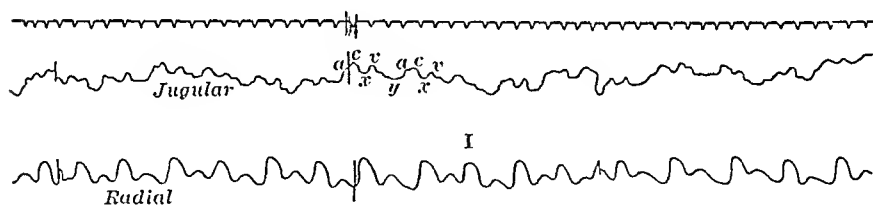


FIG. 6

FIGS. 4, 5, and 6.—Phlebograms taken two weeks, four weeks, and six weeks after operation. Note the shortening of the a - c interval, the progressive diminution of the negative phase y , and the appearance of a first negative phase with its corresponding wave v separating it from the negative phase y in Fig. 6. In the tracing before operation only one negative phase was present;

Brauer's work has changed the diagnosis of adhesive pericarditis from an academic problem into one with a practical therapeutic corollary. The systolic retraction at the apex, the diastolic shock, epigastric diaphragmatic tugging, Broadbent's sign, and cardiac and pulmonary immobility are well known and do not require

discussion here. Pick's pseudo-cirrhosis of the liver gives us a clinical picture which varies from the typical pericarditis. Insidious onset, ascites which rapidly recurs after puncture, intermissions and remission with signs of involvement of the pericardium, characterize the condition. There are two varieties of the disease described. In one type, the true Pick's pseudo-cirrhosis of the liver, the adhesive pericarditis appears to be the causative lesion, the result of which is a chronic stasis of the liver and portal systems, and the formation of an indurative (cirrhotic) nutmeg liver. *The pericarditis* may be well concealed by the other more apparent manifestations. In the polyserositic type we find the iced liver (Zuckergussleber), in which there is a distinct chronic peritonitis.

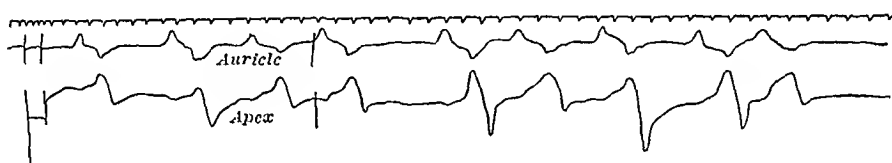


FIG. 7.—Tracing taken from the exposed auricle and from the apex two weeks after operation.

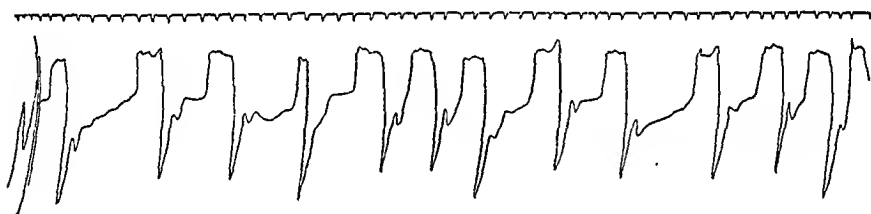


FIG. 8.—Tracing taken direct from the apex three weeks after operation.

In the former class operation is indicated, but where there is evidence of extensive chronic peritoneal inflammation, surgery is contraindicated as far as the mediastinopericarditis is concerned. Our case partook somewhat of the true Pick's cirrhosis type. There was a large ascites with relatively less edema of the feet. The liver was large and hard, and did not regain its normal size until three weeks after the operation. The disproportion of liver and portal stasis to stasis elsewhere was also true of Wenckebach's case.

It is well briefly to review some of the pathological physiology of adhesive mediastinopericarditis. In normal respiration, as the diaphragm moves downward, the abdominal contents are carried downward and forward following the descent of the diaphragm. During expiration the contents move upward and backward. This downward movement of the diaphragm presses the blood out of the liver like squeezing a sponge. The heart moves up and down with the excursion of the diaphragm; in the words of Keith: "The lungs carry their pump with them." According to Wenckebach,

the following disturbed functions result in mediastinopericarditis: (1) The descent of the diaphragm is markedly inhibited. (2) During inspiration the diaphragm pulls at the heart and *via* the heart at the chest wall, at the root of the lungs and at the posterior mediastinum. (3) The heart and large vessels being fixed to their surroundings, inspiration produces a worse condition than expiration. (4) Respiration becomes defective in all of its factors. Deficient movement of the diaphragm and impediment to inspiratory action due to anchoring of the diaphragm results. In this connection Wennekebach⁵ emphasizes the absence of forward movement of the chest as an important diagnostic sign of adherent pericarditis. This author believes that the process of respiration profits by the operation much more than the heart action. In our case the deficient movement of the chest in respiration was striking. The epigastrium seemed to be sucked in with inspiration rather than protruded, and the anteroposterior excursion of the chest wall was slight.

The scope of this paper is too limited to take up in detail the numerous interesting phenomena incident to adherent pericardium. We have purposely avoided the complex problem of diagnosis, for which the literature seems adequate. We wish merely to call the attention of American physicians and surgeons to the procedure by reporting a case in which the result to date (December 1, 1912) has justified operative intervention.

A fairly comprehensive view of the subject may be obtained by consulting the following bibliography:

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⁵ British Med. Jour., 1907, i, 63.

THE RELATION OF PARASITIC AMŒBÆ TO DISEASE.¹

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INTRODUCTION. Within the last seven years it has been definitely proved that the parasitic amœbæ of man, or entamœbæ, are divided into several distinct species, one of which is a harmless commensal; that all cultural amœbæ which have been thoroughly studied are free-living species having nothing in common with the parasitic species, and that the latter have not been cultivated.

These new developments in our knowledge of amœbæ necessitate a revision of some of our data connecting these organisms with disease in man, for all of the evidence gained by experiments on animals or man with cultural amœbæ must be discarded, as such evidence is of no value as showing the relation of parasitic amœbæ to disease in the human subject. In addition, the results obtained experimentally in animals by feeding or injecting material containing entamœbæ must be revised in the light of the proved existence of a harmless and at least two pathogenic species.

Classification of Amœbæ. In considering the relation of entamœbæ to disease in man it is necessary to have a clear understanding of the classification of amœbæ in general. Loesch placed the amoeba he found in man in the genus *Amœba*, calling it *Amœba coli*; in 1879, or four years after the discovery of *Amœba coli*, Leidy established the genus *Endamœba* for the parasitic amœba of the cockroach, described by Butschli under the name *Amœba blattæ*; in 1897, Casagrandi and Barbagallo, after a thorough study of the amœbæ occurring in the intestine of man, became convinced that they differed both in morphology and life cycle from those occurring free in nature, and, apparently unaware of Leidy's genus *Endamœba*, established for the human parasites the genus *Entamœba*. While eventually it may be determined that the spelling of Leidy must be retained, I prefer at the present time to accept the name *Entamœba* for the parasitic amœbæ, as this term has been accepted and is used by almost every writer upon the subject.

After the researches of Casagrandi and Barbagallo, numerous attempts were made to separate the entamœbæ into distinct species, but it was not until 1903 that a clear description was given of at least two species of entamœba occurring in man. During that year, Schaudinn published his work upon parasitic amœbæ, and

¹ Published with permission of the Surgeon-General of the United States Army. Read before the XV International Congress of Hygiene and Demography, Washington, D. C., September, 1912.

differentiated two species: One, a harmless parasite, which he named *Entamoeba coli*; the other, the cause of a form of dysentery, which he named *Entamoeba histolytica*. I was able to confirm Schaudinn's work in 1905, and it has since been confirmed by many protozoölogists in various parts of the world. Recently Prowazek found this species in dysentery cases in Samoa, and states that at no time in its cycle of development were cysts observed at all resembling those found in other parasitic species, but only the spore-like bodies described by Schaudinn.

A third species of entamoeba was described by Viereck in 1906. This parasite, which he named *Entamoeba tetragena*, occurred in cases of dysentery contracted in Africa, and his researches, as well as those of others, proved it to be a pathogenic species, and that it has a wide geographical distribution in the tropics and subtropics, as well as in temperate climates. I have found this species in cases of dysentery contracted in the Philippines, Panama, and in New York, Illinois, Arkansas, and Wisconsin. At the present time some authorities believe that this species is identical with *Entamoeba histolytica*, but the point is far from proved, and until it can be shown that the process of reproduction by gemmation and spore-formation, described by Schaudinn as characteristic of *Entamoeba histolytica*, and confirmed by myself in many cases of dysentery, occurs also in *Entamoeba tetragena*, and that cases of *tetragena* infection occur which never present the characteristic four-nucleated cyst at any stage of the disease process, I am forced to consider the two species as distinct, despite the fact that the nuclear structure of *Entamoeba tetragena*, during certain stages of development, resembles very closely that of *Entamoeba histolytica*.

In addition to the three species mentioned, several others have been described in man, as *Entamoeba tropicalis*, Lesage; *Entamoeba minuta*, Elmassian; *Entamoeba nipponica*, Koidzumi; *Entamoeba williamsi*, Prowazek; *Entamoeba hartmanni*, Prowazek; and *Entamoeba polecki*, Prowazek. It is generally believed that most, if not all, of these species are founded upon insufficient data, and that eventually they will be found to be identical with one or the other of the three species already mentioned.

It may, therefore, be stated that at the present time most authorities recognize three distinct species of entamoeba as parasitic in man, that is, *Entamoeba coli*, *Entamoeba histolytica*, and *Entamoeba tetragena*. These species have been carefully studied by numerous investigators in many parts of the world, and are based upon marked differences in morphology and in the reproductive cycle. The nuclear structure of each species is distinctive, while *Entamoeba coli* forms cysts containing eight daughter nuclei, this number being sometimes exceeded: *Entamoeba tetragena*, cysts containing four daughter nuclei; and *Entamoeba histolytica*, cyst-like bodies, which are budded from the parent organism. In all these species

the differences in the method of reproduction have been carefully studied, and, in my opinion, constitute the most important basis of specific differentiation.

The classification of the amœbæ that have been cultivated from the feces of dysenteric patients and from the pus of liver abscesses is in a most unsatisfactory condition. Several species and subspecies have been described by Whitmore, Walker, Williams, Werner, and others, but no agreement has been reached as to their exact specific status. For long regarded by Musgrave and Clegg, Walker, La Sage, and Noc as true parasitic species, identical with the species of *entamœba* which have already been mentioned, these cultivated amœbæ have been shown to be free-living species of the *limax* type by the more recent work of Hartmann, Werner, Whitmore, Walker, Liston and Martin, Wells, and the writer. All the cultural species that have been thoroughly studied contain a contractile vacuole, an organelle which is not present in any of the parasitic species of man, and they also differ greatly in their reproductive cycle. This subject will be referred to later in the discussion of the relation of these cultural species to disease.

Relation of Entamœbæ to Disease. The following theories have been held regarding the relation of entamœbæ to disease in man: (1) That they are all harmless commensals; (2) that they are secondary factors in the etiology of disease; (3) that all species of amœba are capable of causing dysentery, and (4) that both pathogenic and non-pathogenic species are parasitic in man.

Recent researches have shown that the latter theory, that is, that pathogenic and non-pathogenic species of entamœba are parasitic in man, is correct. It is still impossible to say whether some other factor is necessary before the pathogenic species can cause disease, but the evidence all points to the contrary opinion. At the present time it is generally accepted that certain species of entamœbæ are capable of producing dysentery, but a few authorities still maintain that these parasites are only secondary invaders of the tissues, and are not responsible for the lesions present. In support of this contention they point to the fact that entamœbæ are found in many healthy individuals and in patients suffering from diseases other than dysentery; that dysentery occurs in epidemic and endemic form in regions where entamœbæ cannot be demonstrated; that many different agents when injected into the intestine are capable of producing lesions like those of amœbic dysentery; that direct infection of either animals or man with entamœbæ has never been proved; that the deductions based upon animal experiments are unsatisfactory, and that until we are able to cultivate the entamœbæ and to produce dysentery with pure cultures we are not justified in claiming that they are the cause of the disease.

These objections, with the exception of the last mentioned,

can all be answered by the results of work accomplished during the last few years. We know that the presence of entamoebæ in health and in diseases other than dysentery is explained by the occurrence of a distinct species which is non-pathogenic and which is a parasite of man; that the occurrence of endemic and epidemic dysentery in regions where entamoebæ have not been demonstrated is due to the group of dysentery bacilli; that the lesions produced by the injection of either chemical or bacterial substances into the intestine are *not* identical with those produced by the entamoebæ; that direct infection of animals with entamoebæ has been abundantly proved, and that such experiments *are* reliable when properly controlled. As regards the last objection, that is, that until pure cultures are obtained the causative relation of entamoebæ to disease cannot be maintained, it may be stated that this is not a fair or valid objection, as there are other parasites well known to be the cause of specific infections which have not as yet been cultivated.

In support of the etiological relation of certain species of entamoebæ to dysentery we have the following facts: (1) The absolutely characteristic pathology of amœbic dysentery and the constant presence of the pathogenic species of entamoeba in the lesions and their absence from the lesions of other forms of dysentery; (2) the constant presence of pathogenic entamoebæ in the tissues of the peculiar form of liver abscess which often complicates amœbic dysentery; (3) the production of typical amœbic dysentery in susceptible animals by feeding and inoculation experiments with material containing the pathogenic entamoebæ and the demonstration of the parasites in the lesions so produced.

It is not necessary at this time to discuss in detail the pathology of amœbic infection. It is a self-evident fact to all who have had experience with amœbic dysentery at the autopsy table that the lesions of this disease are absolutely characteristic and are entirely distinct from those of the bacillary forms of the disease. I have had the opportunity of studying hundreds of cases of both amœbic and bacillary dysentery at autopsy, and can state that one may easily distinguish the lesions produced by the entamoebæ from those due to other causes.

If sections are made through the lesions in the intestine, entamoebæ may be demonstrated in every portion of the involved region. They are frequently numerous in the mucous, submucous, and muscular coats of the intestine, where they may be demonstrated in the glandular tissue, in the intermuscular septa, and in the lymphatics and bloodvessels. Of course, in the intestine it cannot be denied that a portion of the pathological picture may be due to bacteria which have gained entrance to the tissues along with the entamoebæ, but the fact remains that the latter organisms are always associated with a characteristic ulcerative lesion never produced by bacteria alone.

I believe that if we had no other evidence than the peculiar lesions of this form of dysentery with which are always associated the pathogenic species of entamœba we would be justified in considering the latter as the cause of the disease.

It is well known that a peculiar form of liver abscess frequently complicates amœbic dysentery. The pathology of this condition is characteristic, and in the contents of such abscesses entamœbæ can always be demonstrated, and if sections are made of the abscess wall these organisms are found within the tissues. Frequently the abscess contents are sterile save for the entamœbæ, while the most careful staining of the tissues fails to reveal any other etiological factor.

The experimental production of dysentery in susceptible animals with entamœbæ dates back practically to the discovery of these parasites. Loesch produced the disease in a dog by the rectal injection of fecal material containing entamœbæ, and his results were confirmed upon cats by Hlava, Kovacs, Kartulis, Zancoral, Strong and Musgrave, and many others. Huber produced dysentery in dogs by feeding them feces containing entamœbæ, and Kruse and Pasqualle produced the disease in cats with the pus from an amœbic liver abscess. The work of Harris, which has been largely overlooked by writers dealing with this question, was of great interest and importance. He endeavored to produce dysentery in dogs by the rectal injection of various bacteria and fecal material from dysentery cases. Among the bacteria injected were the typhoid bacillus, colon bacilli, anthrax bacilli, pyogenic cocci, the dysentery bacillus of Shiga, and mixed cultures of bacteria from dysentery patients. His experiments were most carefully controlled, and in not a single instance did the animals show any evidence of disease following the injection of the bacteria. On the other hand, the injection of fresh feces containing entamœbæ, in the rectum of puppies, was followed in every case by a typical dysentery resulting in the death of the animal experimented upon. In two of the animals amœbic abscess of the liver developed and entamœbæ were recovered from the abscess pus. In all of the animals, four in number, the lesions present in the intestine were typical of those found in amœbic dysentery in man. The period of incubation varied from three to six days. Sections of the intestine of the infected animals exhibited the microscopic pathology of amœbic dysentery, and the entamœbæ were demonstrated in the tissues.

All the experimental work cited, while conclusive as to the production of dysentery in susceptible animals with material containing entamœbæ, is inconclusive as regards the exact species used in the experiments, as these researches were made before Schaudinn's work in species differentiation. Since his observations, however, numerous investigators have proved that

Entamœba coli is not a pathogenic organism, and that *Entamœba histolytica* and *Entamœba tetragena* are the species most frequently concerned in the etiology of amœbic dysentery.

Relation of Entamœba Coli to Disease. *Entamœba coli* is a species frequently observed in the feces in both health and disease. Although it is probably world-wide in its geographical distribution the percentage of infection varies greatly in different localities, being highest in tropical countries and lowest in cold climates.

Schaudinn found it present in 50 per cent. of healthy individuals in West Prussia; in 20 per cent. in Berlin, and 66 per cent. of healthy people examined on the shores of the Adriatic Sea; Vedder, in 50 per cent. of healthy American soldiers, and 72 per cent. of Filipino scouts in the Philippines; Sistrunk, in 11 of 145 patients suffering from diseases other than dysentery in the Mayo Hospital at Rochester, Minnesota, the patients coming from different parts of the United States; and Ashburn and the writer in 71 per cent. of healthy American soldiers in Manila. In 1905, I examined over 200 American soldiers in San Francisco, who were recruited from different parts of the United States, and found that 65 per cent. of them showed *Entamœba coli* in the stools after a saline cathartic. This species has lately been demonstrated by Stiles in North Carolina, by McCarrison in India, and its occurrence in the Philippines confirmed by Whitmore and Walker. It has also been found upon the Isthmus of Panama by Darling and James, in South America by Elmassian, and in Samoa by v. Prowazek.

That this organism is not pathogenic has been proved by many investigators. Its common occurrence in healthy individuals, in whom it has been observed for months and even years without producing symptoms of diarrhea or dysentery, and the negative result of animal experiments by numerous investigators proves that this species is a harmless commensal of the human intestine. Negative results were obtained by Kartulis, Kruse and Pasquale, Celli and Fiocca, Strong and Musgrave, Kovacs, and Jürgens by injecting material containing entamœbæ parasitic in healthy individuals, and Schaudinn showed that this entamœba, which he called *Entamœba coli*, is capable of living in the intestine, but that it never produces symptoms of diarrhea or dysentery either in animals or man.

I have made many attempts to produce dysentery in kittens with *Entamœba coli*, both by injecting fecal material containing them into the rectum, and by feeding material containing both the encysted and vegetative forms, but have never been able to produce the least symptom of dysentery, although 50 per cent. of the kittens given rectal injections of feces containing *Entamœba histolytica* and 65 per cent. of kittens fed with milk infected with material containing the same species developed severe dysentery.

In a recent personal communication Doctor Creighton Wellman

has furnished me with some data regarding experiments with *Entamæba coli*. He infected five kittens by injecting 4 to 5 c.c. of feces containing encysted *Entamæba coli* into the rectum. All the animals remained perfectly well, and were killed about one month after the injection. In none of them were any evidences of dysenteric lesions found at autopsy.

From the evidence which has accumulated it may be positively stated that *Entamæba coli* is not a pathogenic parasite, and that it has been found in a considerable proportion of healthy individuals in every region where it has been carefully searched for. This parasite is chiefly of importance because of the liability of confusing it with the pathogenic entamœbæ, and there can be no question that hundreds of cases of so-called amœbic dysentery have really been diarrheas due to other causes, but so diagnosticated because of the finding of *Entamæba coli* in the stools.

Relation of Entamæba Histolytica to Disease. I have already mentioned the numerous instances of the production of dysentery with material containing entamœbæ, but Schaudinn was the first to demonstrate the actual species concerned in many of these experiments. This species he named *Entamæba histolytica*, and he conclusively proved that it is the cause of a form of dysentery, and that the so-called spores of this parasite are infective. He thus describes his experiments which prove this point:

"From this case I took a small quantity of feces, divided it into three parts, dried each in the air, and mixed with it sufficient water for about twenty crush preparations under cover-glasses. These preparations were carefully examined, the examination being conducted upon a mechanical stage, and requiring many hours. No forms resembling the cysts of *Entamæba coli* were found, but the small spores of *Entamæba histolytica* were noticed in large numbers, but no vegetative organisms could be demonstrated. The cover-glasses were then removed, the feces washed with distilled water, and ten such preparations were mixed with enough distilled water to form 1 c.c. of the mixture. The feces of the animal to be experimented upon, a healthy, strong, young cat, was carefully examined for amœbæ, and none could be demonstrated. To this cat I gave the 1 c.c. preparation mentioned above, mixing it with milk. On the evening of the third day the cat passed bloody mucoid feces, and an examination showed the presence of great numbers of typical *Entamæba histolytica*. In the afternoon of the fourth day the cat perished. Dissection showed typical ulcerous dysentery of the large intestine, and immigration of the amœbæ into the epithelium could be easily established.

"I will mention yet another experiment which goes to prove that the permanent spores by themselves are capable of producing a new infection. The feces of the cats developing dysentery contained only vegetative stages of the amœbæ, no spores being

found. When large quantities of the feces were given to a cat it remained well and for four weeks showed no amœbæ in its feces. It was then fed with the remnant of the dried feces used in the first experiment, which contained multitudes of the spores, and after six days the amœbæ began to appear in the feces. Being older and larger than the other cat it proved more resistant to the infection and did not die until two weeks later. The autopsy showed the lesions of typical amœbic dysentery."

Schaudinn's work served to explain the negative results of some observers with *Entamœba histolytica*. During the active stage of dysentery only the vegetative forms of this species occur in the feces, and as these forms are not infective by feeding, the experiments in which only material containing these forms are used will give negative results. However, if the feces from cases which are recovering from dysentery are used for experimental purposes a large proportion of susceptible animals will develop the disease, as at this stage of the disease the infective spore-like cysts are present.

In 1905, I was able to confirm Schaudinn's work regarding the pathogenic nature of *Entamœba histolytica*. Half-grown kittens were used in my experiments, and 50 per cent. of those given rectal injections developed the disease, while 66 per cent. of the feeding experiments were successful. It will be noted that the latter method gave the best results, as eight of the twelve kittens experimented with developed dysentery, *Entamœba histolytica* being found in the feces and in sections of the diseased intestine. One of the animals developed an amœbic abscess of the liver, and this species of entamœba was found in the abscess contents as well as in sections of the abscess wall. The period of incubation varied from six to fourteen days, being slightly shorter in the feeding experiments than after rectal injection.

All the kittens experimented upon were carefully examined for amœbæ prior to the experiments, so as to rule out a previous infection. Both pure and mixed cultures of all bacteria that could be cultivated from the feces were fed and injected in order to control the tests, and in none of the kittens so treated did symptoms of diarrhea or dysentery develop, and at autopsy no lesions were found in the intestine.

In dysentery produced by the rectal injection of the infected material the lesions were usually localized in the rectum, and were not so severe, as a rule, as when the infection was acquired through the mouth. The lesions produced were typical of those occurring in amœbic dysentery in man, and varied in extent and severity with the length of time the infection lasted. The symptoms consisted of diarrhea, with the passage of blood-stained, mucous stools, containing multitudes of motile *Entamœba histolytica*; rapid emaciation with loss of appetite and strength; and

finally, death from exhaustion. In a few instances attacks of severe diarrhea were followed by a period of constipation, and the disease became chronic in nature. The longest period of incubation was fourteen days in a kitten injected per rectum, and the shortest period six days in an infection by the mouth.

The following protocols of autopsies will illustrate the lesions produced in kittens by *Entamæba histolytica*:

Kitten No. 1. This kitten was injected per rectum on October 19, and killed upon November 21; the first evidence of infection having appeared about October 30.

Autopsy: Body that of a half-grown kitten, greatly emaciated. The abdomen is greatly distended with gas. The mucous membrane of the anus appears swollen, and a considerable amount of blood-stained mucus is adherent to it. The subcutaneous fat has almost entirely disappeared, and the muscles appear dry and atrophied. The pleural cavities are free from fluid, and the lungs appear normal. The heart is greatly congested, and contains red clots in all the chambers. The liver is hypertrophied, deeply congested, and marked albuminoid degeneration is present, but there is no trace of abscess formation. The kidneys are congested, and upon section present the usual lesions of an acute parenchymatous nephritis. The omentum contains a small amount of fat, and is not inflamed. The bladder is filled with urine. The intestines are greatly dilated with gas and fluid. Upon external examination the large intestine appears swollen, is grayish in color, with small, darker colored areas scattered along it. Upon opening the large intestine the mucous membrane of the rectum is found considerably swollen and inflamed, but no ulcerations are present. Above the rectum for a distance of about 10 cm. the mucous membrane is much swollen and edematous, bright red in color, and between the folds a considerable amount of pus can be seen. For a distance of about 4 cm. from the upper end of the large intestine the mucous membrane is inflamed, being red, swollen, and edematous. In this area there are numerous ulcerations, covered in with bloody mucus; they are of small size, somewhat irregular in shape, and extend, in most instances, to the submucosa, although there are a few which extend to the muscular coat of the intestine; the edges are undermined, and many of the ulcers are covered with necrotic tissue, brownish yellow in color, which has to be removed in order to expose them. A few of the ulcers communicate beneath the mucous membrane. The small intestine shows a rather severe acute enteritis and the stomach an acute gastritis.

Kitten No. 3. This kitten was fed once with feces containing *Entamæba histolytica*, and seven days later developed diarrhea, the feces containing blood and mucus as well as numerous motile amoebæ. At the end of two weeks it died, having presented severe symptoms of amoebic dysentery during this time.

Autopsy: Body that of a half-grown kitten, greatly emaciated. Subcutaneous fat entirely absent, and muscles dry and much atrophied. The abdominal cavity is free from fluid, and the intestines appear normal externally. The pleural cavities are free from fluid, and the heart and lungs appear normal. The liver is brownish red in color externally, with irregular yellow motlings. There is a small abscess present at the dome of the right lobe, measuring 0.25 cm. in diameter, showing distinctly through the capsule of the organ. Upon section of the liver the cut surface appears greatly congested, the lobules are distinct, and no abscesses are found other than the one mentioned. The gall-bladder appears normal. The kidneys appear enlarged and congested, and upon section show an acute congestion, with some thickening of the cortex. Externally the large intestine appears slightly, if at all, congested, although the walls are markedly thickened. Upon opening the large intestine it is found filled with fecal material mixed with a large amount of pus and blood-stained mucus. About 1 cm. from the anus, which is blood-stained and covered with mucus, there is an area measuring 4 cm. in length, presenting the typical lesions of amœbic dysentery, as they are observed in man. The entire mucous membrane is swollen, congested, and edematous. Numerous nodular areas project into the lumen of the intestine, which, when incised, are found filled with a glairy material containing hundreds of *Entamœba histolytica*. There are also numerous ulcerations, more or less irregular in shape, with thickened and undermined edges; many are covered in with necrotic tissue which, upon being removed, show that the floor of the ulcer is formed by the muscular coat of the intestine. Many of these ulcers communicate with one another beneath the mucous membrane, and most of them have penetrated to the muscular coat. The remainder of the large intestine presents numerous ulcerations, typical of those seen in the intestine of patients who have died of amœbic dysentery. The lesions are most marked just below the ileocecal valve, where large areas of the mucous membrane have been destroyed, the muscular coat of the intestine being exposed.

Kitten No. 5. This kitten was fed with milk containing *Entamœba histolytica* several times before dysentery developed. The period of incubation was eight days from the date of the last feeding, but from that time until it was killed, three weeks afterward, the animal presented the symptoms of amœbic dysentery, there being gradual loss of appetite, emaciation, and a diarrheal discharge containing blood and mucus, with numerous motile *Entamœba histolytica*.

Autopsy: Body that of a half-grown kitten, much emaciated. Subcutaneous fat entirely absent and muscles much atrophied. The pleural cavities are free from fluid and the lungs and heart

appear normal save for congestion. Upon opening the abdominal cavity the small intestine appears congested externally. The liver is hypertrophied and greatly congested. The kidneys are congested and enlarged, and upon section show the lesions of an acute parenchymatous nephritis. The large intestine is dark gray in color externally, and is considerably thickened, especially toward the rectum. Upon opening the intestine it was found to contain much fecal material, mixed with blood, mucus, and pus. Commencing at the rectum and extending for about half the length of the large intestine the mucous membrane is greatly swollen, bright red in color, and contains numerous ulcers. The majority of the ulcers are spherical in shape, the edges are undermined and greatly thickened, and many are covered in with necrotic tissue. Upon removing this necrotic material the base of the ulcer is found to be formed by the muscular coat of the intestine. The ulcers present are typical of the amoebic ulcerations seen in the intestine of man in every respect. The remainder of the large intestine is black in color and gangrenous, the mucous membrane having been almost entirely destroyed, exposing the muscular coat throughout this portion of the intestine. About 4 cm. below the ileocecal valve there was a small perforation measuring about $\frac{1}{6}$ cm. in diameter.

The following interesting cases of experimental infection with *Entamæba histolytica* have been furnished me by Doctor Wellman. His data cover five kittens, of which four developed dysentery and one remained free from the disease:

Kitten No. 18. On August 20, 1910, 4 to 5 c.c. of feces containing the cysts of *Entamæba histolytica* were injected per rectum. The kitten remained apparently healthy until September 1, when entamœbæ were found in the feces. From this time on the animal grew steadily worse and the number of entamœbæ increased. The animal was killed September 21, and the following conditions were found at autopsy: Great emaciation; heart and lungs normal; liver enlarged, but with no abscesses. Kidney showed signs of nephritis. The mucous membrane of the large intestine was inflamed and edematous, and there were numerous small ulcerations, scrapings from which showed many entamœbæ. The small intestine and the stomach appeared to be somewhat injected. Doctor Wellman stated, "I should call the condition found a typical amoebic dysentery."

Kitten No. 19. The same technique was employed in infecting this kitten. The animal developed dysentery, and *Entamæba histolytica* were found in the feces. The autopsy record of this animal is not given.

Kitten No. 20. This kitten was fed with 4 to 5 c.c. of the same feces used in infecting the kittens already mentioned. After eight days entamœbæ were found in the stools, and the animal died on

the fifteenth day after infection. The following conditions were found at autopsy: The kitten was much emaciated; heart and lungs normal; liver swollen and congested, but showing no abscesses. The kidneys showed the evidences of nephritis. The mucous membrane of the entire large intestine showed typical amœbic ulcerations many of them burrowing in character. The scrapings from the ulcers showed numerous entamœbæ. The entire intestine appeared edematous.

Kitten No. 23. This animal was fed with the same feces, and entamœbæ appeared in the stools on the ninth day after feeding. It was killed on the eighteenth day after infection and the same condition found as in kitten 20, but the lesions were not quite so severe.

Kitten No. 24. This animal was fed with the same feces, but with negative results. No entamœbæ appeared in the feces, and no lesions were found in the intestine when the kitten was killed on the twenty-eighth day after feeding. This animal was considerably older than the others experimented with, and I have found that for successful results young kittens must be used, as full-grown cats are much more resistant to amœbic infection.

Wellman states in his letter that he considers the lesions produced experimentally in these kittens as identical with those of amœbic dysentery in man. More recently Werner, working at the Sailors' Hospital, in Hamburg, has produced dysentery in cats with *Entamœba histolytica*.

He experimented with two strains of *Entamœba histolytica*, only one of which he found infective. He was able to produce dysentery in cats with this strain, but found that after six passages the organism lost its virulence. The incubation period varied from four to thirteen days, the average being nine days. Of six cats infected with this species four died, the duration of the disease varying from seven to twenty-four days, the average being fifteen days. The animals were infected per rectum. Werner states that the lesions were typical of amœbic dysentery, and were always confined to the colon, especially the lower portion. Guinea-pigs and rats were found to be resistant to infection with this parasite.

From the evidence which has been submitted I believe it is impossible to conclude otherwise than that *Entamœba histolytica* is the cause of a form of amœbic dysentery. The character of the lesions present in this condition, the constant association of this species with the lesions, and the production of similar lesions in susceptible animals with material containing *Entamœba histolytica* I consider conclusive proof that this parasite is a cause of amœbic dysentery in man.

Relation of Entamœbæ Tetragena to Disease. The experiments of Viereck, Hartmann, and Werner prove that this species produces a form of dysentery, although Hartmann believes that it is

not as pathogenic to cats as *Entamœba histolytica*. The incubation period in his experiments varied from eight to ten days, and the infection lasted from three weeks to one month. He states that at autopsy the cats presented the typical lesions of amœbic dysentery as observed in man, and that *Entamœba tetragena* was found in the tissues. Darling in a personal communication, states that cats infected with *tetragena* show a severe *enteritis*, especially in the ilium, and not a colitis, which I believe serves to distinguish the lesions of *tetragena* infections from *histolytica*, in which there is always ulceration of the colon; in his infections he evidently was not dealing with *Entamœba histolytica*.

Werner experimented with five strains of *Entamœba tetragena*, only three of which were found to be pathogenic. One of these was still infective after five, one after three, and one after one passage through cats, but they all lost their virulence after repeated passage. The incubation period in his animals varied from five to twelve days, and the disease lasted from three to twenty-five days, the average being seventeen days. He states that he did not find any marked differences between the lesions produced by *tetragena* and *histolytica*, and that he does not believe that the evidence supports the idea that one is less pathogenic than the other.

Werner describes an interesting experimental case in which a cat infected per rectum with a strain of *tetragena* developed dysentery after five days' incubation, the stools containing many entamœbæ. At the end of twelve days the animal died, and at autopsy typical amœbic ulcers were found in the lower portion of the colon, while the right lobe of the liver showed an abscess the size of a hazelnut upon the anterior surface. The pus from the abscess contained entamœbæ of the *tetragena* type.

Franchini reports the production of dysentery in a monkey by rectal injections of fecal material containing *Entamœba tetragena*. The monkey experimented upon had been under observation in the laboratory for over a year, was perfectly healthy, and repeated examinations of the feces before the experiment showed them to be free from entamœbæ. After the rectal injections of material containing *Entamœba tetragena* the animal developed an intense dysentery, the stools containing blood, mucus, and multitudes of entamœbæ identical in morphology with those injected. The animal died from the infection, and at autopsy ulcers were found in the large intestine, and *Entamœbæ tetragena* were demonstrated in sections of the diseased tissues.

In a personal communication, Dr. H. B. Fantham states that he was successful in producing dysentery in one of two kittens fed upon feces containing *Entamœba tetragena* from an infection contracted in Algeria. The kitten died in three weeks, and ulcerations were found in the intestine, which contained *Entamœba*

tetragena. His experiments in kittens with rectal injections of material containing this parasite were all negative.

I have had no personal experience with the experimental production of dysentery in animals with this species, but I consider the evidence sufficient to prove that it is capable of causing the disease in susceptible animals, and that it is a frequent cause of dysentery in man. I have found *Entamœba tetragena* in patients suffering from dysentery contracted in the Philippine Islands, Panama, and several of the United States.

Relation of Cultural Amœbæ to Disease. As several authorities have reported instances of the production of dysentery in animals with cultures of amœbæ, it is necessary to consider briefly this phase of our subject. I have already stated that it has been proved by numerous investigators that all cultural amœbæ that have been thoroughly studied belong to the genus *Amœba* and differ in morphology and life-cycle from the parasitic species belonging to the genus *Entamœba*, and that there is no sufficient proof that any of the latter species have been cultivated.

Prior to the work of Musgrave and Clegg several authorities claimed to have produced dysentery in cats with cultures of amœbæ, while others were unsuccessful in thus producing the disease. It is unnecessary to consider here the conflicting results obtained by such investigators as Kartulis, Vivaldi, Cassagrandi and Barbagallo, and Zaubitzer along this line, but the work of Musgrave and Clegg deserves special consideration. These authors were successful in cultivating numerous strains of amœbæ in symbiosis with bacteria from the feces of dysenteric patients and from liver abscess pus. They refused to accept the classification of Schaudinn, and considered that all amœbæ might, under certain circumstances, become pathogenic. They were successful in producing ulcerations of the intestine and liver abscess in monkeys with mixed cultures of their amœbæ and various bacteria, and in one instance they claim to have produced amœbic dysentery in man with a pure mixed culture of amœbæ isolated from the stools of a dysenteric patient.

In the light of present knowledge these experiments of Musgrave and Clegg have no value as showing the relation of entamœbæ to disease. The work of Hartmann, Werner, Whitmore, Walker, and the writer has proved conclusively that the amœbæ cultivated by these authors are not entamœbæ but free-living amœbæ, and the species with which Musgrave and Clegg claim to have produced dysentery in man is a typical free-living amœba of the *limax* type. The occurrence of dysentery after the administration of this culture can be explained in many ways: The culture may have become infected with the cysts of *tetragena* or *histolytica*, or the person may have become naturally infected or have been infected at the time of the experiment, for in a region such as Manila natural infections would be very difficult to guard against. As regards the lesions

produced in monkeys with cultures of amœbæ, it should be remembered that these animals suffer naturally from amœbic infection, and there is no evidence in the authors' papers that repeated examinations of the animals' stools were made for a sufficient period of time before the experiments to prove their freedom from entamœbæ.

The occurrence of dysentery in monkeys after feeding or injecting cultural amœbæ is probably explained, in the vast majority of instances, by the fact that at least two species of entamœba are parasitic in monkeys, as shown by Castellani and v. Prowazek, and that these species are capable of producing dysentery in these animals. Greig and Wells have also shown that in India natural amœbic infection in monkeys is very common; thus every one of fifty-three monkeys with which they desired to experiment showed amœbæ in the feces which resembled those found in man. These organisms only appeared at irregular intervals, so that repeated examinations of the feces were necessary in order to demonstrate them. Some of the animals presented symptoms of dysentery while under observation, while others appeared perfectly healthy. I do not know the percentage of monkeys infected with entamœbæ in the Philippines, but I personally observed three naturally acquired amœbic infections in these animals in Manila, and I have no doubt that careful examinations, covering a sufficient period of time, would demonstrate that a considerable percentage of monkeys in these islands harbor entamœbæ which could easily be confused with those parasitic in man.

In many of their (Musgrave and Cleggs) experiments the amœbæ were grown in symbiosis with the typhoid bacillus, and this mixed culture was injected directly into the liver, subcutaneous tissue, or the abdominal cavity of the animals used, and was followed by the appearance of abscesses containing both amœbæ and bacteria. It is well known that the typhoid bacillus is capable of producing abscesses when thus injected, and I have myself observed the formation of abscess of the liver after the injection of pure cultures of this organism into the organ, so that deductions based upon such experiments are valueless as proving the pathogenicity of any amœba. Even though lesions were produced in animals with these cultures of amœbæ, they would bear no relation to the disease as it occurs in man, because the cultivated amœbæ are entirely distinct from the true parasitic amœbæ which cause dysentery in man. Personally, I believe that some of the lesions described by Musgrave and Clegg were produced by the mixed cultures of amœbæ and bacteria with which they worked, but I cannot admit that the cultural amœbæ are identical with the parasitic species or that their experiments are of any value as showing the relation of the entamœbæ of man to disease.

The claim of Musgrave and Clegg that the differences in structure and life-cycle of the cultural amœbæ are due to artificial surround-

ings cannot be accepted. Walker in discussing this argument very justly says, "that while slight modifications might occur under such conditions, it is very improbable that cultivation could cause a complete reorganization of the structure of the nucleus, develop *de novo* such a constant organelle as a contractile vacuole, or profoundly modify the life-cycle of the organisms. Moreover, that the supposed modification should invariably take the form of a change from the characters of the genus *Entamœba* to those of the genus *Amœba* is, to say the least, improbable."

It is not difficult to explain the occurrence of free-living amœbæ in cultures made from feces, liver-abscess pus, or from the intestine at autopsy, if one remembers that the cysts of these species are present in the atmosphere, and may thus easily contaminate the cultural material. The recent observations of Liston and Wells prove that it is possible to secure cultures of free-living species of amœbæ upon media exposed to the air, the organisms in such cultures agreeing in morphology with those obtained in cultures from the feces and intestine. Though it is possible for the free-living species to pass through the intestinal canal of animals in an encysted state and afterward develop in cultures, it should be remembered that unless the most careful cultural technique is used such amœbæ may contaminate the cultures from the atmosphere, and it is probable that this is the manner in which many cultures have been obtained, especially in regions where the free-living species are found abundantly. However, it is very difficult to understand how anyone possessing accurate knowledge of the morphology and life-history of amœbæ could mistake these cultural species for any of the entamœbæ of man.

The recent work of Williams, Wherry, and others showing that under abnormal stimulation by adding various substances to culture media, free-living or cultural amœbæ may assume appearances resembling the morphology of the entamœbæ, is of no value for in not a single instance has the nuclear structure of the cultural forms been transformed into that of the entamœbæ of man.

CONCLUSIONS. The following conclusions appear to be justified as regards the relation of entamœbæ to disease.

1. *Entamœba coli* is a harmless commensal in the human intestine.

2. *Entamœba histolytica* and *Entamœba tetragena* are pathogenic species capable of producing in man the disease known as amœbic dysentery.

3. *Entamœba coli*, *Entamœba histolytica*, and *Entamœba tetragena* are strictly parasitic species and have not been cultivated.

4. There is not sufficient evidence at present to prove that any of the amœba that have been cultivated are pathogenic to man. All cultivated species belong to the genus *Amœba*, and differ greatly in morphology and life-cycle from the parasitic amœbæ, which belong to the genus *Entamœba*.

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BREAST TUMORS, WITH SPECIAL-REFERENCE TO CARCINOMA.¹

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TUMORS of the breast constitute a group of conditions presenting considerable variety and requiring great care on the part of the clinician in establishing an accurate diagnosis. The point of chief importance is to recognize malignancy when it exists and to make the diagnosis at the earliest possible moment in order that the patient may have the benefit of surgical intervention at a time when operation holds out the best prospect of cure.

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These tumors may be divided into two great groups—namely, the newgrowths, and those of inflammatory origin. Inflammation, both acute and chronic, is exceedingly common, giving rise to abscess formation or to mastitis without suppuration. Specific inflammatory conditions are those dependent upon the infective virus of tuberculosis, syphilis, or actinomycosis. Cystic tumors exist in the form of galactoceles, such as may originate in the lactiferous ducts or in the gland acini, or a cyst may form as a phase in the development of a newgrowth; an intracystic papilloma is not uncommon, and closely associated from the point of view of etiology is the cystic development found in the ordinary fibroadenoma. Dermoid cysts and hydatid cysts are sometimes found. The benign growth of most frequent occurrence is the adenoma or adenofibroma, presenting considerable variety in the development of the fibrous and epithelial elements respectively in individual tumors. Other simple growths are occasionally met with, such as angioma, myxoma, and lipoma. A mixed tumor resembling that found in the parotid gland has also been described. The malignant growths are usually cancer, but sarcoma develops in a small percentage of cases.

The breast is seldom the site of secondary growth, but metastatic tumors do occur in rare instances. Thus Plew recently reported a case of metastasis in the left mamma in a patient with pelvic sarcoma. He quotes 7 cases from the literature, 5 of these being carcinoma and the other 2 sarcoma. In my own clinic there was an example of secondary cancer in the breast, the primary growth being in the pelvis probably ovarian in origin. In this instance I had used the injection of ascitic fluid recommended by Hodenpyle a few years ago, and some of the injection had been made into the submammary tissue, so that there was some doubt as to whether it was a case of true metastasis or of implantation carcinoma.

While it is obvious that great variety is displayed in the development of newgrowths in the mammary gland, nevertheless the distinctive differences between the two great groups of benign and malignant tumors constitute by all odds the most important material for our study. Every effort should be made to define the cleavage where it exists between these two classes. The ultimate resources of laboratory investigation and clinical observation must often be combined in order to arrive at an accurate diagnosis. The clinical picture of advanced malignant disease is often too conclusive without further investigation being necessary, but frequently patients present themselves with a tumor of the breast where it is impossible to say from the clinical standpoint alone whether it is malignant or not, and again we must view with suspicion the pathologist who undertakes to exclude malignancy with absolute certainty by the examination of a "quick section" at the time of operation. Such an examination must necessarily be

incomplete when made while the operation is in progress. The positive report of the pathologist at such times is of the greatest possible importance but a negative report is of comparatively little value especially when taken apart from the clinical manifestations.

When we take into account all the methods at our disposal for arriving at a diagnosis we must come to the inevitable conclusion that today mistakes in diagnosis are much more common than are justifiable. I am sure that the experience of any general surgeon will coincide with mine in this regard and one who has the oversight of a surgical service in a large hospital must conclude, from the material that comes to his hand, that patients with breast tumor are not studied with sufficient care. The result is that incomplete operations are often undertaken or the terrible results of waiting for definite symptoms of malignancy become all too obvious before the surgeon is consulted. It is mainly because these facts have impressed themselves upon me very forcibly that I ventured to suggest a discussion on breast tumors before the Canadian Medical Association, with the hope that practitioners throughout the country might be awakened once more to their responsibility in this matter, and that further effort might be stimulated to increase our efficiency in the treatment of those unfortunates who are the victims of malignant disease of the breast.

The material which I have utilized for my observations include cases occurring in the various services of the Toronto General Hospital for eight years, from 1905 to 1912 inclusive, to which I have added cases from my private records. These cases may be summarized as follows:

MALIGNANT GROWTHS.

Toronto General Hospital cases:	Carcinoma	158	
	Sarcoma	3	
		<hr/>	161
Private cases:	Carcinoma	54	
	Sarcoma	1	
		<hr/>	55
Total			<hr/> 216

BENIGN GROWTHS.

Toronto General Hospital cases:	Fibroadenoma	58	
	Chronic mastitis	32	
		<hr/>	90
Private cases:	Fibroadenoma	17	
		<hr/>	17
Total			<hr/> 107
Grand total			<hr/> 323

A few observations of statistical value may be made from a study of these 323 cases.

Age. In malignant cases the oldest patient operated on was aged seventy-seven years, the youngest was aged twenty-eight years. The average age was 49.2 years.

Taken in decades the following table was constructed:

30 and under	3.4 per cent.
31 to 40 inclusive	17.5 per cent.
41 to 50 inclusive	40.0 per cent.
51 to 60 inclusive	19.0 per cent.
61 to 70 inclusive	14.0 per cent.
Over 70	5.6 per cent.

In benign cases the oldest patient operated on was aged sixty-one years, and the youngest was aged nineteen years. The average age was thirty-seven years.

Taken in decades the following table was constructed:

20 and under	3.0 per cent.
21 to 30 inclusive	23.0 per cent.
31 to 40 inclusive	38.5 per cent.
41 to 50 inclusive	27.7 per cent.
51 to 60 inclusive	6.0 per cent.
Over 60	1.5 per cent.

Sex. Of malignant cases there were 211 females and 5 males: Married females, 77 per cent.; single females, 21 per cent.; males, 2 per cent.

Where the record of childbearing had been made by the historian one found that there had been no children in 7 cases and one or more children in 54 cases.

Of benign cases there were 105 females and 2 males: Married females, 51 per cent.; single females, 49 per cent.

Of the 5 cases of malignant growth noted in the males 4 were carcinoma and 1 sarcoma. In 2 of these cases of cancer in the male there was a definite history of trauma. In 1 there had been a bruise followed by ulceration, and in 1 irritation of the nipple by braces, causing induration, followed by cancer development.

The history of this latter case in the male extended over thirteen years. He was aged fifty-two years, when he was operated upon for malignant tumor of the right breast; at the time of this operation trouble had existed for seven years. The breast and tumor were removed. Recurrence occurred locally and in the axillary glands, and he was operated on by the writer one year after the primary removal. He died of recurrence five years afterward.

In the case of the man suffering from sarcoma there had been a tumor in the breast for three years, which began to grow rapidly two months before operation. The axillary glands were not involved.

Clinical Manifestations of Malignancy. In making an excerpt of the histories of the 216 cases of malignant growth an effort was made to determine the relative frequency of certain manifestations of cancer of the breast by observing the number of times certain features were recorded by the historians. The following is the result in the order of frequency.

1. Tumor: Present in all cases.
2. Glandular involvement: Axillary glands involved and palpable in 36 per cent. Axillary glands noted as not involved in 6 per cent. Subclavicular glands involved and palpable in 1 per cent. Supraclavicular glands involved and palpable in 2 per cent.
3. Pain: Recorded in 24 per cent.
4. Skin involved: (That is, from mere puckering to marked involvement) 23 per cent.
5. Trauma given as a cause: 12 per cent.
6. Ulceration: In 9 per cent.
7. Retracted nipple: Noted in 6 per cent.
8. Discharge from the nipple: Noted in 5 per cent. In half of these cases the discharge was bloody and in the remainder the character was not stated.

9. Sore nipples in the previous history: This was usually described as "cracked nipple," and was recorded in 3 per cent.

It is noteworthy that the most obvious features in the clinical history of patients presenting themselves with malignant trouble of this kind consisted of a tumor in the breast, with palpable glands in the axilla. Pain was frequently complained of, and there was often more or less involvement of the skin. These were the signs of malignancy which were emphasized as the most significant manifestations of malignancy by our predecessors a quarter of a century ago. By them too retraction of the nipple (which was noted in 6 per cent. of my cases) was considered a most important sign. We should not wait for such signs. It is true that in a given case these conditions will manifest themselves sooner or later, but by that time all chance of saving the patient's life in the vast majority of cases will have disappeared. Unfortunately there are practitioners still who wait for the more certain signs of malignancy before sending their patients to the surgeon. I trust that all will join with me in urging that the qualified practitioner of today who advises his patient to wait for the grosser signs of malignancy is most seriously—I had almost said criminally—negligent.

Let us now inquire into the methods at our disposal in making a diagnosis. At the outset we must admit that a definite diagnosis is often impossible. There are, on the one hand, certain cases of malignant growth which simulate the benign and it is equally true that a benign growth may present features suggesting malignancy. A case, however, which seems doubtful when we first see

it may often be diagnosticated correctly when we use all the means at our disposal to establish the diagnosis.

The age of the patient should make us suspicious. We have seen that the largest proportion of patients with malignant disease are aged between forty and fifty years; nevertheless, we have patients under thirty years as well as very aged women with breast cancer. The character of the tumor itself and its immediate connections must be carefully examined. The cancer growth, usually single and very firm, moves with the breast tissue and not independently of it. At an early period the skin over the tumor is not as freely movable as it is over the normal breast tissue. This test should be tried in a very delicate fashion, placing the fingers on either side of the growth and sliding the skin over it in various directions. The development of the tumor causes a pull upon the ligaments of Cooper, and this puckers or dimples the skin more or less definitely when one attempts to slide it from side to side. The atrophy of the subcutaneous fat immediately over the tumor has also been described as a cause of this puckering. This test can be elicited long before any demonstrable infiltration of the skin and subcutaneous tissues by the growth has occurred. It is not necessary to refer in particular to invasion of the skin, with or without ulceration, phenomena which are characteristic of advanced cancer. Retraction of the nipple too is in evidence as a rule in late cases only. When it is present it is a very strong argument in favor of malignancy. Bloody discharge from the nipple has been looked upon by some as pathognomonic of cancer, but in rare instances a duct papilloma may give rise to it. In a recent paper published by Mintz, of Moscow, the author reports 7 cases of bloody discharge from the nipple and had previously reported 8 cases of serous discharge which he calls "catarrh of the mamma." From his microscopic examinations after amputation he is led to conclude that both forms of discharge indicate proliferative changes in the gland resulting in adenomatous growth or actual carcinoma. Hence, he advocates radical treatment in all these cases. Both forms of discharge, he points out, develop about the climacteric, when involution of the mamma begins.

Both breasts should be examined. The existence of a tumor in each breast is in favor of a diagnosis of a simple growth, but one must assuredly note that there may be a cancer in each breast. Thus in my series there were 4 cases of bilateral development of carcinoma.

The lymph nodes in the axilla are invaded at an early date. No matter how early we operate it is rare for the pathologist to fail to find cancer in the axillary lymph glands. These glands too are, one believes, much more frequently palpable than our clinical records would lead us to suppose. The axilla should, therefore, be explored most carefully by the examining finger in order to

determine whether or not these glands can be felt. Halsted reports 2 cases where cancerous axillary glands due to malignant disease in the mamma, had attained conspicuous dimensions before the breast tumor appeared.

The history as to the duration of the tumor is of little or no value in helping us to a diagnosis. Thus of those cases that came to operation in my series one finds a history extending over varying periods. The shortest was one week and the longest twelve years. The history as to this point in benign cases is very similar.

Turning now to the constitutional effects of malignancy, apart from the local trouble. Emaciation and the cancerous cachexia are symptoms the significance of which is all too obvious in late cancer. It is well, however, to inquire as to loss of weight because even in doubtful cases we occasionally have our suspicions confirmed by a definite positive history in this regard. On the other hand, cancer sometimes exists for a long period without any obvious failure of nutrition. An attempt has been made in recent years to determine whether or not examination of the blood would yield some information of diagnostic value. We do not refer to the kind of blood analysis for which so much was claimed by the plaintiff in a recent famous lawsuit in England, regarding which, in spite of the finding of the Court, I think we may safely assume the test to be of no scientific value. The study of hemolysis for diagnostic purposes has attracted some attention. Thus Weil and Crile have used human serum and human corpuscles for the purpose. In Crile's cases hemolysis was not obtained in 125 normal cases but was observed in 82 per cent. of cases of carcinoma. Whittemore at a more recent date obtained hemolysis in 7 out of 109 normal cases (17 per cent.), while in 22 cases of carcinoma it occurred in 8 cases only (36 per cent.). Hemolysis also occurred in 50 per cent. of tuberculous cases and was found also in Hodgkin's disease, chronic empyema, etc. These results would lead one to believe that the test is of little diagnostic value. Weil showed that while the serum of cancer patients was destructive to normal red cells, the red cells of cancer patients are more or less resistant. Crile states that while the test must not be considered as a specific, yet he believes it to be of diagnostic value particularly in early cases, in all of whom, he thinks a hemolytic serum exists. A complement-fixation test, similar in principle to the Wassermann reaction, has been employed, using the antigen of carcinoma cells. The test is useless in diagnosing syphilis from cancer as the sera of the former are sometimes positive to this test. Lastly, it has been found that normal sera have the power of breaking up cancer cells *in vitro*. It is, therefore, obvious that the study of the blood yields results which may have a very significant bearing on the question of establishing a diagnosis of cancer. In the meantime, however, we cannot say that the specific value of the blood test has been definitely determined.

In doubtful cases at the time of operation one may employ the method introduced by Stiles, of Edinburgh, known as the "nitric acid test." It is as follows: "Place a sliced lump in 5 per cent. solution of nitric acid for a few minutes and then wash in running water; the epithelial elements will be rendered opaque by the coagulation of the protoplasmic epithelial cells, while the connective-tissue elements are rendered more or less translucent or gelatinous. By observing the amount, arrangement, and distribution of the epithelial elements one can almost invariably say if it is cancer or a mastitis or hypertrophy of the ultimate globules of the gland parenchyma."

Again we may obtain a report from the pathologist at the time of operation by removing a portion of the growth for the purpose. This is the so-called "quick section." The surgeon waits for the report from the pathologist and completes the operation according to the findings. Or, again, the breast and tumor may be removed and the wound closed; the pathologist then makes a careful and complete examination of the tissues, and if malignancy is found the radical operation is completed a few days later. These operations for diagnostic purposes should, however, be avoided if possible. Most surgeons agree that there is considerable risk of disseminating the disease by manipulations of this kind. At all times in operating for malignancy we should handle the breast very gently and disturb the diseased tissues as little as possible while we make our incisions wide of the trouble through healthy tissue. A deliberate incision through the focus of cancer is by no means devoid of danger. It is far less reprehensible to do the radical operation with a mistaken diagnosis of malignancy than it is to spread the disease more widely in our effort to secure an absolutely accurate diagnosis. Again we should be on our guard when we receive a negative report from the pathologist who examines a quick section. We cannot agree with Rodman who states that he always relies upon frozen sections in hospital practice. Such a report is by no means conclusive, when positive findings of cancer are not made. Let me illustrate by reference to a case in my own practice:

Mrs. A. A., aged forty-nine years, had a lump under the nipple of the left breast for three years. Increased rapidity of growth occurred shortly before she consulted me. There was no retraction of the nipple but an axillary gland was palpable. I proceeded at once and did the radical operation. It happened that the axillary gland was lost for a time in the laboratory and the pathologist (a most competent and experienced worker) reported that the breast tumor was not malignant. Subsequently the axillary gland was found and on section proved to be malignant. A careful and prolonged search was now made of the breast tumor and eventually an undoubted focus of malignancy was found, which had hitherto escaped observation.

Such a case illustrates the futility of trusting to a negative report in a frozen section. It further emphasizes the importance of making a most careful search through all growths which appear benign in the first series of sections. Different parts of the tumor should be searched for evidence of malignancy before a final verdict is given. The conditions here may be compared to those found in the prostate gland where we believe malignancy is much more common than we had hitherto imagined. Careful search of the so-called "enlarged prostate" not infrequently demonstrates the existence of a focus of cancer which had not been suspected and somewhat similar findings are recorded in tumors of the mammary gland.

Another suggestive case occurred in my series, in which a patient, aged forty-nine years, had a growth removed from the breast which was reported as an adenoma by the pathologist. She returned seven months afterward with what proved to be a recurrent carcinoma at the site of the former operation.

Bloodgood is reported as saying at a recent meeting of the American Medical Association: "In my experience after one has had a sufficient training, the diagnosis from the gross appearance is easier, quicker, and in many cases more certain, than from a rapid frozen section."

If, therefore, with the most skilled assistance in establishing a diagnosis, and after using all the means available to that end, we are occasionally misled, we are inevitably driven to the conclusion expressed in the surgical axiom: "Any lump in any woman's breast is better out than in" (Finney). Greenough and Simmons come to a similar conclusion in the study of fibroepithelial tumors of the mammary gland.

The fact that malignant degeneration of benign growths in the breast is of frequent occurrence is obviously another convincing argument for the removal of all breast tumors. A recent study by Speese showed that no less than 26 per cent. of the cases of chronic cystic mastitis (that is, that form of "abnormal involution" occurring at the menopause) examined by him showed malignancy. So too cyst adenomas are found associated with carcinoma, the frequency of such association being placed by some authors as high as 15 per cent. Inflammatory conditions of the breast resulting in mastitis are often found in the early history of cancer cases. All these facts point conclusively to the frequent occurrence of malignant degeneration in benign growths of the breast.

Operative Treatment. The so-called "radical operation" should be carried out in all cases of malignancy. The skin incisions should vary in direction with the individual case, and should be so planned that a wide area is removed leaving an ample margin round about the site of trouble. The whole breast and both pectoral muscles (except perhaps the clavicular portion of the pectoralis major),

with the fat, fascia, lymph vessels, and glands of the axilla, are removed *en masse*. It is not necessary to dwell in detail upon the steps of such an operation because the technique is fully described in all modern text-books and the necessity for such radical procedure is practically universally admitted.

One is forced to believe that the part of the radical operation which is not done with the degree of thoroughness, which is so essential, is the removal of the gland-bearing fascia and fat along with all lymphatic tissue having connections with the mammary gland. The principal lymphatic channels of the mamma pass to the axillary group of glands. While this is fortunately the case one must remember that other channels exist through which the disease may be disseminated. Oelsner and Poirier have demonstrated undoubted connection between the internal mammary group within the thorax and the breast by means of a small lymph channel traversing the great pectoral muscle and passing through the fourth interspace at the level of the costochondral articulation. Fortunately these glands are not frequently involved, a circumstance which may be accounted for by the atrophy of this channel in senile mammae, in which cancer usually develops (Poirier). The subclavicular glands are more likely to be involved. Rotter and Stiles have demonstrated the actual spread of cancer through the great pectoral muscle along afferent vessels, which, having perforated that muscle, run between it and the pectoralis minor and reach the subclavicular group of glands. These lymph channels accompany the thoracic branch of the axillothoracic artery. The writer has recently demonstrated the implication of these glands in 2 cases when operating before his clinical classes. Grossman has succeeded in injecting these lymphatics in the dead subject. Implication of this group is much more likely to occur where the pectoral muscle is invaded by the cancer growth. Obviously, therefore, we have here a strong argument in favor of the routine removal of both pectoral muscles and of a thorough clearance of the uppermost part of the axillary space. The axillary vein and often the lower part of the subclavian must be cleaned thoroughly in the dissection. In rare instances the vein has been sacrificed. Thus, Stiles has removed portions of the axillary and Strunikow has recently reported 2 cases in which he resected the subclavian vein. In these cases there was only temporary edema of the arm.

The work of Sampson Handley has called special attention to the route of visceral invasion in breast cancer and he has given convincing demonstration of the spread from the primary focus along the lymphatic plexus of the deep fascia to the epigastric angle, where through the parietes immediately below the ensiform cartilage invasion of the abdominal cavity occurs. Thus we are forced to believe secondary deposit in the liver occurs and by this

route, too, Handley thinks we may have secondary invasion of the pelvic viscera (for example, ovary or uterus), once the peritoneal cavity has been reached, the action of gravity accounting for the fact that secondary tumors are found most abundantly at the lower limits of the serous cavity. These observations of Handley have induced the writer to follow his practice and to extend the field of operation so as to remove the fat and fascia over the epigastric triangle with the object of safeguarding the possible visceral invasion from that area.

Results. The best statistics available indicate that we are dealing here with a most treacherous and deadly disease. Stiles in the discussion before the British Medical Association, in 1908, stated that from 40 to 50 per cent. were permanently cured if a thorough operation were done. Cheyne, some eight years ago, claimed 57 per cent. of cures, his figures being based on the supposition that a cure was assured when a period of three years had elapsed after operation without recurrence. The three-year limit had been suggested by Volkmann. Jonas, in 1907, showed that 56.7 per cent. of his cases were free from recurrence after three years. Barker, on the other hand, claimed that 30 per cent. of those living three years after operation died of cancer. The fallacy of basing a claim for permanent cure after the lapse of three years is obvious to all. Many of us could report recurrence after an interval of eight, nine, or ten years of apparent immunity. Steinthal, of Stuttgart, has recently published a paper in which he gives statistics of three series of cases. The first series had been reported in 1905 and again in 1908, the second series in 1908, and all three series were tabulated in a paper written this year. The first series, therefore, was published at three-year intervals on three successive occasions. The percentage of cures claimed in the milder cases of the first series was 78.5 per cent., but this dropped in 1908 to 71.4 per cent., and in 1911 to 64.2 per cent. In the more severe cases the percentage of cures claimed in 1905 was 29.4 per cent., in 1908 it was 26.4 per cent., and in 1911 it had fallen to 23.5 per cent. Similar facts are elicited in the other series to show that if these cases are followed up and late recurrences recorded we shall find that our statistical tables based on short-time limits are of little value. Steinthal has expressed the opinion that between 25 to 30 per cent. of all cases are permanently cured by operation.

Korteweg at the Surgical Congress at Brussels enunciated a somewhat paradoxical thesis that the prognosis in cancer was the more favorable the later it was operated upon. By which he apparently meant that if a cancer had existed for a prolonged period without apparent increase or spread, then a radical operation would hold out a better prospect of permanent cure than would be the case were the operation done early. The statistics of Steinthal do not, however, support this theory, and I fancy

it is one which will not appeal to us as a safe guide for our treatment of these cases. It is apparently true that there is an attempt at natural cure in carcinoma. Sampson Handley believes this is brought about by a perilymphatic fibrosis.

We are familiar with the complete fibrosis which occurs in those rare cases of so-called "atrophic scirrhus," in which the patient lives on and may finally die of some intercurrent disease. I might refer to a patient who came under my observation who died at the age of eighty-three and who was known to have had cancer of the breast for twenty years, but which showed no sign of active growth until a few months before she died.

Spontaneous disappearance of cancer has occurred in rare instances. Hitherto effort made to discover some agent which would promote the natural arrest of cancer has proved unavailing. The effect of the x -rays is disappointing—superficial nodules disappear, but are almost certain to recur. It has been suggested by some that excessive use of the x -rays may be prejudicial, because it is known to destroy leukocytes, and may thus interfere with the inflammatory reaction, which is apparently such an important factor in bringing about a permanent cure. We know little of the permanent effect produced on the tissues by either the x -rays or radium in malignant disease.

Recently, I operated on 2 cases at the instance of Dr. W. H. B. Aikins, who has given a postoperative course of radium treatment: One was a case of carcinoma of the breast in a woman, aged forty-three years, with a tumor of a year's duration, involving the whole breast. It was adherent to the pectoral muscle, and the skin was involved with a mass in the axilla. Operation appeared to hold out little hope of success, but we deemed it worth while to try the combined effect of an extensive radical operation and subsequent course of radium. The other case in which radium was tried was in a woman, aged thirty-seven years, suffering from a sarcoma of the breast. Twenty months prior to my operation she struck the left breast and a tumor developed at the seat of the injury. A short time afterward she became pregnant and a child was born. She used the affected breast to some extent in nursing the child, but the lump became painful, and was incised when pus was said to have been evacuated. Ten days subsequently the lump was removed, and on recurrence after a short interval was again removed. At the time of my operation she had a recurrence in the scar, which was adherent to the pectoral muscles below. There were no glands palpable in the axilla. A radical operation was performed, and Dr. Aikins gave her a postoperative course of radium treatment. It is now four months since the operation, and there is no further sign of local trouble, although a series of rapid recurrences had occurred previously.

It is too early to speak of the result of treatment in these two instances, but when we have a "borderland" case it seems wise to give the patient the benefit of whatever line of action holds out the slightest prospect of relief.

Let me here enter a strong protest against submitting patients to operation where the condition is obviously too far advanced for relief by surgical measures. For example, patients with visceral involvement or with bone metastases are obviously beyond hope of relief. Invasion of the bony framework of the chest wall, or a mass of glands lying above the clavicle are equally hopeless and should not be subjected to operation. These are cases in which we believe the doctrine of Hippocrates holds true when he says that cases of cancer will live a long time if not interfered with by surgical means. In other words, we know that operation in these cases simply hastens the final issue. Let me give you an example of such a case. The history is as follows:

Mrs. X., aged forty-eight years. Ten months prior to consultation she had a bloody discharge from the nipple. A tumor had existed for four months. She now had a tumor implicating the whole breast, with ulceration about the nipple. It was markedly adherent to the deeper structures, with a mass of involved glands in the axillary and subclavicular region. The case was pronounced inoperable, and the patient so advised. She subsequently went to one of the best-known general hospitals in the United States, where a prominent surgeon removed the breast by radical measures, but after resecting part of a rib and finding the pleura involved, he desisted and closed the wound. The patient died in the hospital a few days afterward.

Such cases are better left alone not only for the patient's sake but because such measures strongly impress the laity, and women hesitate to submit to surgical procedures which prove so disastrous.

Some surgeons (for example, Gosset) remove the involved supraclavicular glands after temporary resection of the clavicle, but the hope of radical relief by such measures is so remote that one may discard such a proposition. The practice in the Mayo clinic is more commendable, where if the supraclavicular glands are enlarged it is their custom to excise one under local anesthesia, and if it proves to be malignant, no operation is advised, since it is probable that other and inaccessible regions are involved. (Judd.)

The functional result after the radical operation is remarkably good. It is important, if possible, to save the subscapular nerves and the posterior thoracic, otherwise an important group of muscles will be paralyzed, leading to very marked disability.

The mortality after the radical operation is wonderfully low considering the extent of the procedure. We realize this when we find the late Dr. Maurice Richardson, of Boston, reporting 1500 breast operations, with a total mortality of 4. In the series pub-

lished herewith there was a mortality of 3.2 per cent. after operation for malignant disease of the breast. As these included recurrent cases such as appear in a general hospital clinic, the mortality is not high. In my own private cases there was no operative mortality.

Recurrences. Of the 216 cases of operation for carcinoma of the breast we find that in no less than 42 (19.4 per cent.) were operations undertaken for recurrence. Of these, however, only 8.3 per cent. were recurrent after a radical operation. The following is the summary:

TABLE OF THE RECURRENT CASES WHICH ARE INCLUDED IN THE SERIES OF 216 PATIENTS.

Recurrence after radical operation	18 cases	8.3 per cent.
Recurrences after incomplete operation:		
Breast and axillary glands	1 case	
Breast and tumor	2 cases	
Tumor only	17 cases	
<hr/>		
Total	20 cases	9.3 per cent.
Recurrences but no facts in history	4 cases	1.8 per cent.
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Total cases	42 cases	19.4 per cent.

The youngest patient operated on for recurrence was aged twenty-nine years. The oldest patient operated on for recurrence was aged seventy-seven years. The average age of patients operated on for recurrence was forty-eight years.

The longest period elapsing before operation for recurrence: After radical operation, three years; after incomplete operation eight years.

The shortest period elapsing before operation for recurrence: After radical operation, three months; after incomplete operation, three months.

The average period elapsing after radical operation before the operation for recurrence was performed was 14.2 months.

The average period elapsing after incomplete operation before the operation for recurrence was performed was 23.4 months.

It would obviously not be fair to take this table as indicating the proportionate number of recurrences after the radical operation and after the incomplete operation respectively unless we remember that during the period under review (1905 to 1912) the number of incomplete operations yielding results would be few, because there must necessarily be few surgeons who would do other than a radical operation in cancer of the breast unless indeed there were a mistaken diagnosis. In spite of these facts, however, we find the recurrences after radical operation presenting themselves were fewer than after the incomplete operation. From these figures we may in fact assume that recurrence is a much rarer event after the radical operation than after the incomplete operation.

Another fact which comes out in these statistics is that no fewer than 17 cases came to operation for recurrence where the tumor only had been removed. On going into the history of these 17 cases one is justified in concluding they were cases of cancer when first operated upon. If this be the case then it is indeed time we should protest against the practice, which one fears is much too common, of removing a breast tumor without establishing a definite diagnosis in every instance. If a pathological laboratory is not available in the remote parts of the country where these operations are of necessity occasionally undertaken, then it is a simple matter to send the specimen to some larger centre for pathological report, and then the case may be dealt with according to the findings without undue loss of time.

It will be noted that the longest period elapsing after the radical operation before the operation for recurrence was three years and after incomplete operation eight years. The average period elapsing was after radical operation 14.2 months, and after incomplete operation 23.4 months. The numbers under review are perhaps not sufficiently large for definite conclusions, but they suggest that where recurrence does take place it is more rapid after the radical operation than after the incomplete one. The writer is unaware of any observations on this point. It is obviously one well worth noting, and should be further investigated.

Murphy believes the final results in carcinoma of the breast have not been materially improved in the last quarter of a century. He states that cases that have no demonstrable lymphatic metastases at the time of operation remain well in a considerable percentage of cases exactly as they did with our forefathers who excised breast tumors and did nothing else. He believes, however, that any hope of improvement in our results lies in early recognition and prompt removal of the disease.

In reviewing my series of cases one endeavored to determine the length of time the tumor had existed prior to surgical relief. The following table was constructed:

AVERAGE DURATION OF DISEASE AT TIME OF OPERATION.

Malignant growths: Average duration	14.375 months
(This does not include 2 exceptional cases where the duration was said to have been twelve years. Exclusive of these 2 the longest period was eight years and the shortest one week.)	
Those who came to operation under one year	54.5 per cent.
Those who came to operation under six months	35.4 per cent.
Those who came to operation under three months	19.0 per cent.
Those who came to operation one month and under one month from initial symptoms	8.4 per cent.
Benign growths: Average duration, adenofibroma	15.8 months
(This does not include one exceptional case of fifteen years and another of twenty-four years.)	
Chronic mastitis	2.9 months
(This does not include an exceptional case of thirteen years.)	

It appears to the writer that the foregoing table is significant, showing as it does that nearly 50 per cent. of our patients are allowed to go untreated for a whole year before they come to operation. On the other hand, only 8 per cent. come to us during the first month of trouble. Can anyone doubt that our percentages of cure would be vastly increased were the figures reversed? It is to be hoped that the time is not far distant when women will of their own initiative seek the advice of a practitioner of medicine whenever a tumor of the breast appears and that the doctor in turn will insist upon an immediate diagnosis being made. In the event of cancer being found then the modern radical operation will be carried out with the best possible prospect of saving the life of the patient. The writer is optimistic enough to believe that sooner or later such a desirable state of affairs will be brought about, and then the surgeon will be able to show vastly improved results in the operative treatment of this terrible malady.

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THE RELIEF OF GASTRIC CRISES IN TABES DORSALIS BY RHIZOTOMY.¹

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THOUGH surgery of the spinal nerves is still of comparatively recent origin, nevertheless such remarkable advances have been made in this field during the last few years, and so much suffering and almost intractable pain have been alleviated, that we can scarcely feel too sanguine as to its future. Since Abbé and Bennett, in 1888, first conceived the idea of resecting the posterior spinal roots for the relief of neuralgia of the brachial plexus, similar operations have been performed by Horsley, Chipault, Duplay, and others for the relief of intractable pain. For example, rhizotomy was performed by Faure in a case of inoperable tumor of the uterus and by Giordano for the relief of sciatica. In 1900 Mingazini² proposed intradural resection of posterior sacrolumbar roots in a case of tabes, with severe lightning pains in the legs, but rhizotomy was not performed.

Gastric crises of tabes were described as early as 1851 (Romberg and Grube), but they have been well known only since Charcot's classic description of them in 1868. The excellent researches of Head and others have proved quite conclusively that disorders of this nature are of nervous origin. The crises are oftentimes one of the earliest stages of the disease, and increase in severity until the patient's life is menaced by the excessive denutrition and the morphine habit, to which he almost inevitably is forced to resort, and while life itself lasts, the suffering is so terrible that he is ready to try almost anything which promises relief. Numerous therapeutic measures have been used, such as lumbar puncture, epidural injections of stovain and novocain, the alternating current, and the x-ray treatment, but these have brought sometimes only transient relief and sometimes none at all.

One of the earliest operations for the relief of this condition was carried out by Vallas and Cotte³ in 1906, on a patient who for six years had suffered from lancinating pains and uncontrollable vomiting. The abdomen was opened and the stomach found to be normal; the solar plexus was then freed from the celiac axis and stretched. The crises ceased immediately and did not appear again during the time which elapsed before the case was reported to the Society of Medicine of Lyons, on March 26, 1906. There is no record of this procedure being imitated.

¹ Read before the Philadelphia Neurological Society, April 26, 1912.

² *Neurolog. Centralblatt*, 1910, No. 8.

³ *Révue neurologique*, 1907, p. 27.

In 1908 Förster aroused the interest of surgeons by conceiving the idea of resecting certain posterior dorsal roots in severe cases of crises in which all other forms of treatment had failed. This procedure is justified on the theory that the crises are due to irritation of the sensory sympathetic fibers of the stomach, which, after entering the celiac plexus in the splanchnic major nerve, pass to the spinal cord through certain posterior dorsal roots. This irritation manifests itself in the severe pain and vomiting, in the tremendously increased hyperesthesia of the skin of the epi-, meso-, and hypogastrium, and in the exaggeration of the epigastric reflex. If we concede this hypothesis, and if we agree with Head that the sensory fibers innervating the stomach are the seventh to ninth posterior dorsal roots, then we cannot but acquiesce in Förster's suggestion of resecting these nerves, thus intercepting the sensory pathway to the stomach, to relieve the crises.

On the other hand, it has been proved that the stomach is supplied by sensory fibers from the pneumogastric nerve, representing the central nervous system, as well as by the sympathetic. Eppinger and Hess⁴ came to the conclusion through their physiological experiments that visceral crises are to be explained by irritation and later paralysis of the autonomous nervous system (vagus nerve), thus laying stress on the motor rather than on the sensory irritation. On these grounds Knapp and many surgeons are skeptical as to the value of Förster's operation for the relief of visceral crises, as they think the nerve supply of the stomach is much more dependent on the vagus than upon the sympathetic.

Indeed, during the last year Exner⁵ proposed the resection of both vagus nerves for the relief of gastric crises in tabes, and in order to avoid any untoward complications, he advises that this operation be followed by a gastrostomy and the introduction of a drain from the stomach to the duodenum. After about three weeks the drain may be removed. Exner considers this procedure much simpler than rhizotomy and feels that its results will be even more satisfactory. In his first case, the vomiting and pains in the epigastric region ceased, while the lancinating pains in the legs and the hypogastrium remained. This was the condition three months after the operation. In his second case, the vomiting stopped after the operation, but the pain in the epigastrium was very severe and atony of the stomach was pronounced up to the time of the patient's death three weeks after the operation. Owing to the satisfactory results of his first case, Exner believes this to be the legitimate procedure in severe cases of gastric crises, but the operation, has not yet been repeated often enough to enable one to pass final judgment on it, nor has sufficient time elapsed since the

⁴ Götzl, Wien. klin. Woch., 1910, vol. xxiii, No. 21.

⁵ Deutsche Zeitschrift f. Chirurgie, 1911, xlviii, 1679 to 1682.

performance of the operation to determine what the ultimate results will be.

The observations made in Siding's case, in which an herpetic eruption appeared over the areas supplied by the sixth to ninth thoracic nerves make me feel all the more confident of the splanchnic origin of the crises. Furthermore, Raux,⁶ in his histological researches, found that the fine nerve fibers which connect the dorsal roots to the cells in the sympathetic ganglia were partially degenerated in tabetic subjects; while the strong, medullary fibers originating in the intervertebral ganglia were not decreased to any appreciable extent. A glance at the evolution of these crises adds somewhat to the plausibility of rhizotomy in this connection, for pain and hyperesthesia are the first symptoms to appear, while the motor disorders in the form of vomiting and hypersecretion, follow probably as reflex disorders.

The first rhizotomy for the relief of gastric crises was carried out in 1908 by Förster⁷ and was so successful that the operation has been repeated a number of times since. The patient, a man, aged forty-seven years, having suffered from severe crises for six years, was greatly emaciated and addicted to morphine, and no treatment had been of any avail. The laminae of the fifth to tenth dorsal vertebrae were removed, though the dura was not opened. As no relief ensued, on the next day the dura was opened, and the sixth to tenth posterior dorsal roots were resected. The patient began to gain weight immediately, and there was no return of the crises up to the time of his death nine months later from phthisis.

In another case the patient, who was in a critical condition, had been afflicted with severe crises for ten years, and had lost over sixty pounds. He had undergone two previous abdominal operations, with no benefit. Küttner divided the sixth to eleventh posterior dorsal roots on both sides, and the patient made a complete recovery with no relapse during the two years intervening between the operation and the report.

The first case (File, No 10122), which was brought to my attention had been under the care of Dr. Kingsbury and was seen in consultation by Dr. George P. Müller, to whom I am indebted for the privilege of having operated and presenting this report. The patient, aged forty years, had been suffering for the last three years with attacks of pain and vomiting. The pain was so violent as to double him up, and the attacks recurred every four to six weeks. One year before the operation a diagnosis of cholelithiasis had been made, but an exploratory operation did not reveal any lesion of the upper abdomen. He was admitted to the University Hospital, September 6, 1911, and at that time a careful examination failed to disclose any suspicion of an organic lesion of the

⁶ Neurolog. Zentralblatt, 1901, p. 27.

⁷ Therapie der Gegenwart, August, 1911.

stomach, but certain well-defined symptoms of tabes dorsalis—sluggishness of the pupillary reflex, disturbances of station with eyes closed, absence of patellar and Achilles reflexes on both sides, and considerable hypotonia in flexing the thigh on the abdomen. The gastric phenomena were most pronounced, and the patient welcomed any operation which offered reasonable hope of relief.

Accordingly on September 19 I performed a rhizotomy through a unilateral or hemilaminectomy. A curved incision, beginning at the tip of the spinous process of the third thoracic vertebra and extending to the spinous process of the sixth thoracic, was made down to and through the aponeurosis. This flap was reflected and the muscles separated from the left side of the spinous processes of the fourth, fifth, and sixth thoracic vertebrae. The laminae of the fifth, sixth, and seventh thoracic were removed with rongeur forceps and the spinal canal opened. Before the operation we decided to cut the seventh, eighth, ninth, and tenth sensory roots in the dorsal cord. The seventh root was identified as coming off the cord a little above the tip of the spinal process of the fourth thoracic vertebra. This identification was not difficult, and the plan as above outlined, was carried out, except the tenth root on the right side was left uncut, chiefly because of the difficulty in exposing it. The wound was closed with catgut sutures, a counter opening being left for drainage. The patient's condition at the end of the operation was perfectly satisfactory.

Following the operation there was some weakness in the right leg and retention of urine, but before he left the hospital he had regained vesical control and much of the power in his limb. In a recent communication the patient writes that he has been entirely relieved of the pain and vomiting, and has been gaining steadily some of the forty-five pounds he had lost since the onset of the disease three years ago. On the whole, therefore, the operation has been of the greatest benefit and more than justified itself.

Leaving out of consideration Exner's operation on the vagus nerves and Vallas and Cotte's stretching of the solar plexus, several modifications of the intradural division of the spinal roots have been proposed. For example, Guleke⁸ thinks it is much simpler not to open the dura, but to divide the roots after they have left the dural sac; and Lambret,⁹ after an unfortunate experience, was inclined to agree with him. Guleke operated in 2 cases according to this method, with very satisfactory results, and claims this operation can be performed with greater facility than the intradural method. But I should be inclined to think, and I believe many surgeons will uphold me in this point, that the separation of the anterior from the posterior roots after they have left the

⁸ Archiv f. klin. Chirurgie, 1911, xcv, 495.

⁹ Echo méd. du Nord, 1910, xiv, 589 to 591.

dural sac would be a matter of considerable difficulty, and that there would always be the additional risk of a residual palsy.

At the German Surgical Congress, March 30, 1910, Franke¹⁰ recommended the severance of the posterior roots by avulsion of the intercostal nerves without opening the vertebral canal. His patient made a complete recovery and was able to go about his regular occupation. Von Frankl-Hochwart¹¹ resected the seventh, eighth, and ninth intercostal nerves in a patient suffering from gastric crises, but unfortunately only ten days intervened between the performance of the operation and the end results are not known. But little consideration, I think, should be given to the proposal of Hänel,¹² who claimed that relief may be obtained through a simple decompressive laminectomy alone, and urged that considerable time be allowed to elapse before the second stage of the operation was performed. In his case the crises disappeared after laminectomy, but unfortunately the patient died a few months later. In the experience of Küttner, Tietze, and several others, who perform the rhizotomy in two sittings, no appreciable benefit was derived from the laminectomy, though several weeks had elapsed between the two sittings.

This is not the place nor is there time to discuss at length the minor details of the operative technique, but there are a few features which I think are deserving of mention. In the first place, I do not advocate the performance of the operation in two sittings, a plan to which the German and French surgeons cling. To be sure, the grosser movements entailed in the removal of the laminæ do not fit the hand of the operator for the more delicate coördination required in the subsequent manipulation of the roots, but the advantages of the completion of the operation in one sitting so far outweigh those of the two-stage operation that unless the condition of the patient manifestly does not justify carrying the operation to its conclusion there should be no interruption. That patients in the prone position are more subject to respiratory difficulties under ether anesthesia is a matter of common knowledge, especially in rather prolonged operations; and in this connection I should like to call attention to the value of administering the anesthetic by intratracheal insufflation. To my mind the introduction of this method of administering ether is bound to have a tremendous influence in diminishing the depressing tendencies of the more serious operations, particularly where the patient is compelled to lie on the table face down, as is the case in laminectomies and operations on the posterior fossa. It is not necessary to go over the physiological grounds upon which these beneficial results are based. Suffice it to say that in my own clinical work it has relieved my mind of what once was a very disturbing factor.

¹⁰ Centralblatt f. Chirurgie, 1910.

¹¹ Verhandlungen der Gesellschaft deu. Nervenärzte, 1911, p. 227.

¹² Zeitschrift f. Versicherungsmed., 1910.

As to whether the roots should be exposed by a unilateral or bilateral laminectomy is a matter which should be left to the choice of the individual operator. When the roots on both sides have to be exposed, I am rather in favor of the bilateral exposure, as it gives better access to the structures, facilitates the isolation of the roots, and thereby shortens the operation. It makes not a little difference whether one is at work in the cervical and upper thoracic or in the lower thoracic and lumbar region. The lower down in the canal the deeper are structures from the surface, and the more difficult is it to expose and differentiate the roots through a unilateral opening without traumatizing the cord unduly. In the case included in this report it so happened that I was able to accomplish my purpose by removing only one-half the laminae. But even if the spinous processes and the whole arch of the laminae are resected, it is surprising how little, if any, is either the strength of the back or the comfort of the patient affected.

I have been able to gather from literature the records of 30 rhizotomies for the relief of visceral crises in tabes. Of these, there were 9 complete recoveries, 16 cases in which there has been improvement, and 5 deaths. Though these results are by no means startling, yet it is exceedingly gratifying to realize that 30 per cent. have been entirely relieved and 56 per cent. partially so of a very painful complication for which hitherto there has been no source of relief other than morphine. In cases in which there has been recurrence the crises have been less severe, of shorter duration, and with longer intervals between the attacks. In the case of Bruns and Sauerbruch, in which there was a recurrence six months after the operation, the patient was able to resume his occupation as a mason, and the same was true of the 3 cases operated on by Tietze, in 1 of which a woman who had been bed ridden for two years, recovered sufficiently to be able to attend to all her household duties.

In discussing the results of the operation, a word or two should be said about the mortality and the recurrences. As for the mortality, it should be borne in mind that in a number of instances the patients were anything but fit subjects for operative intervention. Many are exhausted by pain and suffering, many addicted to the morphine habit, always an undesirable situation to deal with, others again are subjects of toxemia from infection of the urinary tract, in fact, 2 of the series died as a result of cystitis. In order that the operation should not meet with disapprobation because of the mortality incident to it, it behooves neurologists and surgeons alike to exercise the greatest discretion in the selection of cases and to advise operation, if at all, in the earliest stages before the patients are rendered unfit by complications above mentioned for an operation, which, though involving no extraordinary risks, must be rated as a major surgical procedure.

In considering the variable results following root resection, attention should be drawn to the experimental work of Kidd¹³ who has already collected a large amount of evidence, surgical, experimental, histological, and embryological, which he thinks leads to the inevitable conclusion that afferent fibers in some cases algetic, in others reflex, exist in the spinal ventral roots of man and many other vertebrates. And he even goes so far as to advocate the division of the ventral as well as the dorsal roots except in the case of the third and fourth cervical roots. The resulting disability would be preferred, he believes, to the continuance of pain.

That the section of a given number of roots should in some cases be attended with complete recovery, in others with only partial recovery, and again in others should be followed by recurrence, is a matter which at once provokes an interesting discussion. Förster attributes the unsatisfactory results to the fact that an insufficient number of nerves have been cut, as the sympathetic nerve fibers originating in the stomach and intestines are very numerous. He therefore recommends that the greatest possible number of nerves be divided, including the fifth and sixth, and eleventh and twelfth, as well as the seventh to ninth, which alone were at first thought necessary. This theory would seem to be substantiated by one of Guleke's¹⁴ cases, in which a relapse occurred after the resection of the seventh to ninth dorsal roots, but when the patient has been subjected to a second operation, at which the tenth and eleventh roots also were divided, there was no further trouble. It may be that Förster's explanation will solve the problem. At least I have found that in many instances recorded as recurrences the pain did not recur in the stomach at all, but was referred to the intestines, that is, to the lower rather than the upper abdomen. It would seem more than plausible, therefore, that we should be able to prevent the subsequent development of crises in the intestinal tract, improperly designated as recurrence, by cutting the tenth and eleventh thoracic, in addition to the roots immediately above. Whether it is necessary in the light of our present knowledge of the nervous supply of the stomach to section the two roots above the seventh—namely, the fifth and sixth—is a matter which can be determined only by subsequent observations and further experience.

If it be true that in some cases the gastric crises of tabes have their origin in some form of irritation of the pneumogastric nerves, it goes without saying that a rhizotomy of the dorsal roots in these cases will be of no benefit whatsoever. The fact that in none of the recorded cases did the patients fail to derive some relief from section of the dorsal roots would seem to controvert this theory.

¹³ British Med. Jour., August 19, 1911.

¹⁴ Archiv klin. Chir., 1911, xcv, 495.

However, if it be true, as I understand to be the case, that neurologists recognize clinically an exceptional type in which the crises are of pneumogastric origin, there should be no hyperesthesia in the cutaneous distribution of the dorsal roots and no increase in the epigastric reflex; and according to the observations of Head, there should be hyperesthesia in the temporal and parietal regions as the sensory fibers of the trigeminus occupy the same segment as those of the vagus. If this clinical differentiation is possible, there should be no difficulty in excluding those cases in which dorsal root resection is contraindicated.

The time has come when those who are interested in the development of surgery in the field of neurology should come to some conclusion as regards the propriety of this comparatively new operation, technically known as rhizotomy, with its varied applications. Laminectomy as an operation has lost many of the terrors with which it was associated in the minds of the past generation. I have had to open the dural sac on a number of occasions for a great variety of conditions, with the loss of only 2 cases—1 a multiple sarcoma of the cord, and the other a root resection in an imbecile child; the death in the former instance was attributed to exhaustion, and in the latter to a very peculiar train of events which did not seem to bear directly on the character of the operation. Personally, I am quite prepared to advocate in most positive terms rhizotomy as a means of relieving pain in suitable cases and where other measures have failed: (1) Because it is based on a sound physiological basis, and (2) because it has been followed by gratifying results in not an inconsiderable percentage of cases.

A CASE OF ALKAPTONURIA.

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NEW YORK CITY.

(From the Herter Laboratory, New York City.)

As alkaptonuria is a congenital anomaly of metabolism rather than a disease its interest must lie mainly in the indications which it may give as to the development of metabolic processes in fetal life or as to the normal oxidation in those substances whose abnormal catabolism it represents. The patients having alkaptonuria present no characteristic symptoms. The only diagnostic alteration in their metabolism which has been discovered is in their failure to normally burn tyrosin and phenylalanin. These sub-

stances, whether they have been taken in the food or built up in the tissues or given experimentally, are converted into homogentisic acid, which is excreted unchanged in the urine. As the cause of this condition is still unknown, and as relatively few cases have been reported¹ (about 60 in all), it has seemed well to add this record to those which have been published.

Mrs. A. J., a widow, aged thirty-one years, applied for treatment November 1, 1910, suffering from vague rheumatoid pains in her back and neck, accompanied by a general feeling of weakness. Ten years ago she was told by a physician she had diabetes.

FAMILY HISTORY. The patient's father and mother were born in Germany. There is no consanguinity in the families of her parents. No history can be obtained of any of her family having urine which darkened on standing or which stained the clothing. Specimens of urine from 9 of her relatives have been examined in connection with this study of her case. None of these contained homogentisic acid. There is a family tendency toward diabetes. One sister and a nephew have a distinct reaction for sugar in the urine. The patient's mother, another sister, a niece, and another nephew had a trace of sugar in the urine. The urine from her father and from two of her sisters was normal. In all these cases of glycosuria, sugar was found both by fermentation and by Fehling's method.

PERSONAL HISTORY. When the patient was aged about one year, her mother first noticed that her diapers were stained by the urine. This was noted more as she grew older, when the urine stained the clothing a "red, brick red or maroon" color. She was well throughout her childhood. Menstruation began at seventeen years. The menstrual blood was sometimes dark, almost black in color; sometimes it was bright red; this darkening of the menstrual blood was probably from admixture with urine. She was married ten years ago. She was never pregnant. Three years ago her appendix and a cyst of the right ovary were removed, and as she had severe backache and metrorrhagia following the operation the left ovary and a part of the uterus were removed later. She has frequent pain in the left eye, the left side of the head, and extending up the left side of the neck. She has frequent numbness in the fingers of the left hand. She is also subject to pain and stiffness in the lumbar region, so that she has to be helped in rising from a recumbent position when she wakes. Some days she has great thirst. The amount of urine varies greatly, and at times she passes excessively large amounts. She sweats freely all the time. Her mentality is normal, but she is neurotic in temperament.

¹ See Garrod, *Inborn Errors of Metabolism*, 1909, and Fromberg, *Neure Forschungen auf dem Gebiet der Alkaptonurie*, *Biochem. Centralbl.*, 1908-1909, viii, 1-9.

PHYSICAL EXAMINATION. The patient is a tall, well-nourished woman, with a dark complexion and black hair. Her usual weight is 125 pounds. The sclerotic coats of the eyes have a grayish tint (ochronosis). There is one small dark spot in the cartilage of the left ear, otherwise the cartilages as well as the finger nails are normal in color. The thyroid gland is slightly enlarged. The heart, lungs, and abdominal organs appear normal. The systolic blood pressure is 120 mm. in both radial arteries. Her pulse rate is 84.

URINARY ANALYSIS. The urine gives the characteristic reactions found in cases of alkaptonuria, which are due to the presence of homogentisic acid, which is a powerful reducing agent and turns brown when it is oxidized. The color of the freshly voided urine is pale yellow. It soon assumes a brownish tint, which slowly darkens until the urine becomes nearly black. When an alkali is added the surface exposed to the air quickly becomes brown and the darkening of the entire specimen is hastened. When ammonia is added to the urine, and it is allowed to stand, it becomes a deep brownish-red color. When the urine is mixed with Fehling's solution the blue color is first changed to green before heating, then it gradually assumes a brown color from the presence of the alkali. On boiling, Fehling's solution is reduced with the formation of a reddish-brown precipitate. The urine rapidly reduces an ammoniacal solution of silver nitrate even when no heat is applied. On heating the urine with Nylander's reagent there is no reduction of the bismuth. There is no yeast fermentation, and the urine is optically inactive. On adding dilute ferric chloride solution drop by drop an evanescent bluish-green color is produced. Homogentisic acid was separated out from the urine and was identified by Dr. H. D. Dakin,² who has reported some experiments in metabolism which he made upon this patient.

General examination of urine, May 12, 1911: Volume, 1140 c.c. in twenty-four hours; color, light yellow; specific gravity, 1021; albumin, negative; indican, slight; indol-acetic acid, slight; *p*-dimethylaminobenzaldehyde reaction, slight; acetone, trace; phenol, marked reaction; sugar, negative.

NITROGEN EXCRETION AND NITROGEN PARTITION. The first specimens of urine were collected when the patient was on a general mixed diet of her own choosing; these showed an excessive nitrogen excretion and an abnormally large volume. Thus on November 22, 1910, the volume measured 4260 c.c., with the total nitrogen 36.8 grams. November 29 the volume was 2900 c.c. and the nitrogen 27.3 grams. The patient was told she was taking too much nitrogenous food, and after that the diet became more normal.

² Jour. Biol. Chem., 1911, ix, 151.

TABLE I.—Nitrogen Partition.

	March 28, 1911.		May 12, 1911.	
	Grams.	Per cent. of Total N.	Grams.	Per cent. of Total N.
Total nitrogen	21.05	10.81	
Urea nitrogen	19.52	92.73	9.74	90.1
Ammonia nitrogen . . .	0.52	2.47	0.43	4.0
Purin nitrogen	0.25	1.19	0.22	2.0
Creatinin nitrogen . . .	0.33	1.57	0.37	3.4
Hippuric acid nitrogen .	0.34	1.61	0.03	0.3
Undetermined nitrogen .	0.09	0.43	0.02	0.2

The nitrogen partition³ was made on two specimens, each representing an average of two days (Table I). The percentage of the various forms of nitrogen in these analyses did not deviate from the normal. The percentage of urea is high showing that there was a rather unusually complete digestion and utilization of the nitrogen of the food. The ammonia excretion is normal or slightly high for normal but not as high as one would expect with so large an amount of homogentisic acid in the urine. This also has been noted by Sehum,⁴ who found only from 5.05 to 6.89 per cent. of nitrogen of ammonia in the urine of his patient. The nitrogen of ammonia was determined on the following days:

January 9, 1911	0.82 grams	4.9 per cent.
January 25, 1911	0.87 grams	4.7 per cent.
March 28, 1911	0.52 grams	2.5 per cent.
May 12, 1911	0.43 grams	4.0 per cent.
September 7, 1911	0.66 grams	3.7 per cent.

The daily excretion of uric acid in the case of this patient varied very widely. In the specimens on which the nitrogen partition was made the amount of uric acid was normal. In a collection made for two days, January 9 and 10, 1911, the daily average was only 0.0087 gram., the nitrogen of uric acid being 0.017 per cent. of the total nitrogen. Wide variations in the amount of uric acid

³ Methods: The homogentisic acid in the urine renders inaccurate a number of the usual methods of urinary analysis. The following methods were used in this case. Duplicate analyses were made in the quantitative determinations.

Total nitrogen: Kjeldahl's method.

Urea nitrogen: Morner und Sjöquist's method (Neubauer und Vogel [Huppert], *Analyse des Harns*).

Ammonia nitrogen, uric acid nitrogen, creatinin nitrogen, and indican. According to Folin (*Amer. Jour. Physiol.*, 1905, xiii, 45), before determining the creatinin the homogentisic acid must be removed by continuous extraction with ether after acidifying with a mineral acid. For the precipitation of the uric acid a small narrow-necked (Ehrlenmeyer), well-stoppered flask was used. In making the ammonia determinations, rapid suction was continued for four hours.

Remaining purin nitrogen after removal of uric acid. Method of Krüger und Schmidt (*Zeitsch. f. physiol. Chemie*, 1905, xlv, 1); modified by Benedict (*Jour. Biolog. Chem.*, 1909, vii, 27).

Sulphur: Benedict's method (*Jour. Biolog. Chem.*, 1909, vi, 363).

Sulphates: Folin's method (*Jour. Biolog. Chem.*, 1906, i, 131).

⁴ *Münch. med. Woch.*, 1904, p. 1599.

excreted have been reported by many writers, the amount having been reported as abnormally low by Embden,⁵ Stange,⁶ and Ogden.⁷

SULPHUR PARTITION. The sulphur partition was determined for five days (Table II). The sulphuric acid combining with aromatic bodies varied widely on the different days, three of the specimens having a low ratio for the aromatic sulphuric acid and one a relatively high ratio ($\frac{\text{H}_2\text{SO}_4\text{I}}{\text{H}_2\text{SO}_4\text{E}} = 7.3$). The neutral sulphur in the urine is normal in amount although the hydrogen sulphide in the feces is above the normal.

TABLE II.—Sulphur Partition.

Date.	Total S as H ₂ SO ₄ .		Total oxidized, H ₂ SO ₄ .		Inorganic, H ₂ SO ₄ .		Etheral, H ₂ SO ₄ .		Neutral, H ₂ SO ₄ .		Ratio: $\frac{\text{Inorganic, H}_2\text{SO}_4}{\text{Etheral, H}_2\text{SO}_4}$.
	Grams.	Grams.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.	Per cent.	
January 9, 1911 . .	3.895	3.469	3.330	85.5	0.139	3.6	0.426	10.9	24.0		
January 25, 1911 . .	3.678	3.302	3.200	87.0	0.102	2.8	0.376	10.2	31.4		
March 28, 1911 . .	3.143	2.771	2.439	77.6	0.332	10.6	0.372	11.8	7.3		
May 12, 1911 . .	2.313	2.016	1.858	80.3	0.158	6.8	0.297	12.9	11.8		
September 7, 1911 .	4.094	3.538	3.385	82.7	0.153	3.7	0.556	13.6	22.1		

AROMATIC COMPOUNDS. In the oxidation of both tyrosin and phenylalanin, in cases of alkaptonuria, the benzene ring is not broken down, but instead homogentisic acid is formed which is itself an aromatic compound. As the essential anomaly in this condition lies in the imperfect oxidation of two aromatic bodies, the behavior of all aromatic compounds becomes of special interest. In the present case tests were made in the urine for the following aromatic bodies: Indican, phenol, total etheral sulphates, hippuric acid, the aromatic oxyacids, and idolacetic acid. The specimens were also tested with the *p*-dimethylaminobenzaldehyde reagent, which reacts with certain aromatic as well as other substances.

There were wide variations in the ratio between the aromatic and preformed sulphates, as has been noted by other observers (Table II). Indican was present in small amounts in some of the specimens and negative in others. The qualitative test for phenol in the acid distillate was sometimes negative and sometimes gave a marked reaction. Hippuric acid was present in normal amounts.

⁵ Zeitsch. f. physiol. Chem., 1893, xvii, 182.

⁶ Virchow's Archiv, 1896, cxlvi, 86.

⁷ Zeitsch. f. physiol. Chem., 1895, xx, 279.

The aromatic oxyacids and indolacetic acid were present in traces. The *p*-dimethylaminobenzaldehyde reaction was very slight. It is thus seen that there was no characteristic variation in the amount of any of these aromatic compounds.

SUGAR TOLERANCE. The urine of this patient as stated above was found to be free from sugar; that is, there was no yeast fermentation and the urine was optically inactive. The sugar tolerance of the patient was tested. One hundred and fifty grams of cane sugar were given and the urine collected for twelve hours from the time of taking the sugar. The urine by fermentation was found to contain a distinct trace of sugar. One hundred and twenty grams of sugar were then given, and the urine collected for twelve hours was found to contain 7.8 grams of sugar. Again, 132 grams of sugar were given, and during the next six hours, 0.3 gram of sugar was found in the urine. It is thus seen that the tolerance for sugar is nearly normal, but it is at times a little low.

FECES, April 18, 1911: Color, dark; reaction, alkaline.

Microscopic Examination: Vegetable fibers, vegetable spirals, oil droplets, starch granules, no meat fibers found.

Bacteriological Examination: Gram-stained smears from the feces appear normal; Gram-negative bacilli are the prevailing form of bacteria. Hydrogen sulphide in the moist feces, 0.032 per cent.

BLOOD EXAMINATION, August 29, 1911: Red blood corpuscles, 3,152,000; leukocytes, 2000; hemoglobin, 78 per cent.; polymorphonuclear cells, 60 per cent.; small lymphocytes, 34 per cent.; large lymphocytes, 4 per cent.; transitional forms, 1 per cent.; eosinophiles, 1 per cent.

The blood coagulates more rapidly than is normal. In a capillary tube, coagulation begins within one and three-quarters minutes, and is complete in two minutes.

The perspiration and ear wax do not give any reaction for homogentisic acid.

The classical symptoms of alkaptonuria which have been noted in this case are the constant presence in the urine of homogentisic acid, the darkening of the sclerotic coats of the eyes and slight darkening of the cartilage of the ear (ochronosis), and the local irritation of the strongly acid urine. Other less characteristic symptoms noted in this case which have been reported in some cases of alkaptonuria are a general weakness, a neurotic disposition, a tendency to rheumatoid pains, and an irritation of the bladder causing an increase of bladder cells and of leukocytes in the urine. Other unusual symptoms of this patient are a rapid coagulation of the blood and a slightly low tolerance for sugar, with a family history of diabetes. It may be worthy of note that the patient is from a German family. The most of the cases have been reported by physicians in Germany, and of those reported from other countries several have been German.

REVIEWS

THE ANATOMY OF THE HUMAN EYE AS ILLUSTRATED BY ENLARGED STEREOSCOPIC PHOTOGRAPHS. By ARTHUR THOMSON, M.A., M.B., F.R.C.S., Professor of Human Anatomy in the University of Oxford. Pp. 131; 67 stereoscopic photographs. London: Henry Frowde, 1912.

THIS contribution to the gross anatomy of the human eye consists of a series of sixty-seven stereoscopic photographs, under a magnification of from two to three diameters, accompanied by a small volume of descriptive text. Although the application of stereoscopic photography to the display of anatomical structures is no longer a novelty, it has seldom been used to better advantage than in the present instance. This satisfactory result, however, depends by no means solely on the stereoscopic effect, but on the combination of the latter with an enlargement sufficient to exhibit details and relations, which are inadequately seen with the unaided eye. Many of the pictures are telling examples of the value of hand-glass anatomy—a method of study too much neglected, now that the microtome and microscope stand ever ready.

The illustrations comprise five groups: (*a*) anteroposterior sections of the eye; (*b*) dissections of the eye from the front; (*c*) anterior half of the eye seen from behind; (*d*) the lens; (*e*) posterior half of the eye.

The first group offers most instructive views of the fibrous tunic, with its variations in thickness and the relations of the sulcus scleræ to the sulcus circularis corneæ. Admirable views are afforded also of the suspensory apparatus of the lens and of the ora serrata; likewise of the optic nerve and papilla. The sections of fetal eyes exhibit the thick cornea, the spherical lens, and the redundant retina, as well as the hyaloid artery.

The dissections of the eye from the front supply instructive pictures of the iris and of the lens, with its striæ shimmering through the pupil. One of the most interesting preparations was made by removing half of the iris, after the sclera and cornea had been cut away, and thus exposing the posterior chamber and its posterior wall. In other preparations the entire iris has been removed, with the cornea and part of the sclera, in this way displaying the complete ring of the suspensory ligament attached to the lens. By

photographing with a combination of transmitted and reflected light, the details of the zonule of Zinn are shown with unusual clearness, the radially disposed suspensory fibers, passing from the inner surface of the ciliary body to the circumference of the lens, appearing with great distinctness.

The ciliary processes, orbiculus ciliaris, and ora serrata are strikingly shown in several photographs of the anterior half of the eye, taken from behind. The quite regular alternation of the larger and smaller ciliary processes is emphasized, as well as the larger number of the folds, from sixty-eight to eighty, than the usually assumed quota. Of the views of the posterior segment of the eye, several are of particular interest, as they show not only the optic disk, physiological excavation, and retinal vessels, but also the macula and the fovea.

The sixty odd pages of text accompanying the plates, although arranged to call attention to the many interesting details to be seen in the photographs, are much more than a mere description of the illustrations, constituting, as they do, an excellent synopsis of the gross anatomy of the human eye, well meriting a careful perusal. A series of leadered outline figures, giving in detail names and relations, forms an adequate key for the identification of the structures shown in each photograph.

The plates, as photographs, are, with few exceptions, excellent, not a few being exceptionally sharp and clear. The difficulty of obtaining such results will be appreciated best by those having had actual experience in photographing preparations in fluid and under magnification.

Professor Thomson has supplied the means of acquiring an understanding of the eye, which should be welcomed not only by students of anatomy, but also by surgeons concerned with the delicate structures of the organ of vision. G. A. P.

THE PRACTITIONER'S VISITING LIST FOR 1913. Pp. 192; 3 illustrations. Philadelphia and New York: Lea & Febiger.

ONE of the most useful aids to the busy physician that has recently come to our notice is *The Practitioner's Visiting List* for 1913. With such a well-arranged and convenient little book ever ready in his pocket the most hard pressed of practitioners should easily be able to keep accurate account of his visits. The book is issued in several styles so as to meet the requirements of even the largest practice.

A valuable feature of this Visiting List is the accompanying text, which contains the information that a doctor continually

needs: for example, a scheme of dentition; tables of weights and measures; a diagnostic table of eruptive fevers; a list of incompatibles, poisons, antidotes, a table of doses, etc.

The excellence of this little book makes it evident that the issue for 1913 will receive the same hearty welcome from physicians throughout the country that has uniformly been accorded the preceding twenty-eight issues.

G. M. P.

PLEURISY. By ALEX. JAMES, M.D., Consulting Physician to the Edinburgh Royal Infirmary. Pp. 240; 4 illustrations, 4 clinical charts, and 19 diagrams. New York: William Wood & Co.

THIS book, which the author states is the outcome of thirty years' experience in hospital and private practice, presents his views on a subject about which he is well qualified to speak, and which he has abundantly illustrated by case-reports. Besides being an able treatise, it has, therefore, the added value of emphasizing in a clear direct style those ideas which are particularly his. He states in the preface: "It may be at once remarked that any reader who considers full reference to medical literature essential in a medical book need not read farther. . . . Rather has it been my endeavor to hand on the broad general truths regarding this disease which the generation to which I belong has inherited, along with what little in the way of illustration, explanation, and augmentation my experience and reading seem to me to be able to add."

The first three of the fourteen chapters discuss the etiology of pleurisy. Then follows a detailed description of pleural effusions, empyema, pleurisy associated with malignant growths, and streptothrix and leptothrix infections. A chapter on treatment closes the work. The consideration of empyema occupies nearly half of the book, there is a chapter on its natural methods of cure, on the relation of empyema to bronchiectatic cavities, on its unusual localizations, on fetid effusions, and on pulsating and phthisical empyemas.

What most attracts interest in the book is the handling of the mechanical problems connected with effusions, the arguments being ingenious, and made lucid by a liberal use of diagrams. Dr. James does not share the generally accepted view that the heart is displaced by the pressure of fluid, believing on the contrary, that when the lung on the affected side relaxes, the elastic traction of the sound lung pulls the heart to the opposite side. His argument is supported by experiment. Of similar interest is the consideration of the bulging and non-bulging of intercostal spaces, of the formation of the S-shaped curve, and particularly of the mode of formation

of bronchiectatic cavities. To the explanations for pulsating empyema already extant, he adds another and very plausible one, supported by a case history and autopsy.

In instances of the delayed reabsorption of serous effusion he strongly advocates allowing the patient to be guided by his own feelings about getting up, putting him to bed only on a return of fever or pain, a practice which has been followed also in cardiac cases with benefit and comfort to the patient. In the treatment of empyema, one is rather surprised at the frequent mention of chloroform, and is led to assume that the use of local anesthesia for this condition is not so common in Edinburgh as it is with us. Evidently "red meat and red wine" is a by-word there, for it is mentioned often in the treatment of the phthisical.

James' *Pleurisy* is interesting reading. It is characterized throughout by its directness and good sense, and its ideas are stimulating, whether one accepts or disagrees with them. H. G. S.

INFANT FEEDING. By CLIFFORD G. GRULEE, A.M., M.D., Assistant Professor of Pediatrics, Rush Medical College, Chicago. Pp. 295; 29 illustrations, and 8 original colored plates. Philadelphia: W. B. Saunders Co., 1912.

THE author considers the subject under four heads: (1) Principles of nutrition including anatomy, physiology, and metabolism; (2) breast feeding; (3) artificial feeding; (4) nutrition in other conditions commonly found in infancy.

Judged by the standards recently set by Continental pediatricians he has succeeded in the difficult task of effectively covering the broad field of the infants' nutrition. This difficulty is greatly increased by the uncertainty which is felt by most American observers as to the underlying as well as active causes of many of the nutritional and gastrointestinal disturbances in infancy.

The author accepts, in large part, the teachings of Finkelstein and Mayer, and divides the gastro-enteric disorders as follows: Weight disturbances (chiefly fat intolerance), dyspepsia (duodenal indigestions, fatty diarrhea), decomposition (marasmus), intoxication (summer diarrhea, ileo-colitis, cholera infantum, dysentery).

The importance of Finkelstein's teaching is generally admitted in America, but it is questionable whether or not we are prepared to agree absolutely with the statement "that the primary cause of the intoxications (see synonyms) is a dietetic one and that the specific action of the pathogenic bacteria is secondary to the primary nutritional defect." If this be true, we must be prepared to hear that true cholera and amebic dysentery are due to dietary

indiscretions, or that the pneumococcus bears no important etiologic relation to pneumonia, because its habitat frequently is found in the air-passages of well persons. Fortunately for the patient, the uncertainties as to etiology do not materially affect the dietetic treatment of the intoxications and the advice on this head is sound and practical, while the great danger of "doing too much" is emphasized by the simplicity and saneness of the advice with regard to drugs and other therapeutic measure. The book will prove to be a most useful one to the student and general practitioner.

J. C. G.

A TEXT-BOOK OF OBSTETRICS. By J. WHITRIDGE WILLIAMS, M.D., Professor of Obstetrics, Johns Hopkins University. Third edition; pp. 946. New York and London: D. Appleton & Company, 1912.

THIS book is so well and so favorably known that an extended review is unnecessary. It has been thoroughly revised and brought up-to-date, and although the author states in his preface that he has been criticised for the inclusion of a list of references at the end of each chapter, it is hard to see how such criticism can be justified. Such an arrangement must be of enormous help to the student and particularly to the busy practitioner, and in our opinion is heartily to be commended. Two criticisms only suggest themselves: The position of the patient in Fig. 310, p. 323, illustrating the proper position for delivery, involves more exposure than is desirable in most cases and does not allow the same facility in protecting the perineum from injury that is afforded by delivery upon the side; and, secondly, nearly all the illustrations of examinations, obstetric operations, etc., depict an operator with bare hands without rubber gloves, an omission that should be corrected in future editions. The illustrations are numerous, exceedingly well executed, really illustrate what they are intended to show, and as an example of the book-maker's art it is hard to see how the volume could be excelled.

J. C. H.

A COLLECTION OF PAPERS PUBLISHED PREVIOUS TO 1909. By WILLIAM J. MAYO and CHARLES H. MAYO. Volume I, pp. 498; 46 illustrations. Volume II, pp. 591; 25 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

DOUBLE frontispieces, showing the two authors as recent graduates and as mature surgeons, are prefixed to these volumes which contain a vast miscellany of reprints on all sorts of surgical subjects.

The earliest papers date from 1884. Some are of only ephemeral interest, and a few of no interest at all; most of them, however, are well worthy of preservation in the excellent form in which they are presented by the competent editor, Mrs. M. H. Mellish.

The first volume contains mostly papers dealing with abdominal surgery. The second volume, besides numerous articles on the surgery of the intestines, includes such various topics as extra-uterine pregnancy, skin-grafting, aneurysm, mastoid abscess, infantile spinal paralysis, brain cysts, fractures, and infections of joints. There are also several "travelogues," and numerous occasional addresses.

All of these articles presumably have long ago reached the audiences for which they were intended, and no further comment is required. The Mayo brothers have passed a busy life, observing keenly, studying industriously, and teaching themselves and others most indefatigably. To see the present volumes as mementoes of work accomplished surely brings its own reward. A. P. C. A.

TRÉPANATION NÉOLITHIQUE, TRÉPANATION PRÉ-COLOMBIENNE, TRÉPANATION DES KABYLES, TRÉPANATION TRADITIONNELLE. Par le Dr. LUCAS-CHAMPIONNIÈRE, Membre de l'Institut (Académie des Sciences), Chirurgien Honoraire de l'Hôtel Dieu, Membre de l'Académie de Médecine, etc. Pp. 136; 32 illustrations. Paris: G. Steinheil, 1912.

LUCAS-CHAMPIONNIÈRE was a pioneer in head surgery. At the commencement of his career, in the sixties and seventies of the last century, the operation of trephining had fallen into great disrepute. He not only undertook to revive it, under antiseptic precautions, and to guide his interventions by the newly established methods of cerebral localization, but he developed the theory of *decompression*, which has later been widely accepted. Now that the passage of years has enabled him to retire from active practice, he employs his time, with characteristic indefatigability, in historical researches such as that now before us.

Prehistoric trepanning, as it is called, was established as a fact in 1868, when certain neolithic skulls were found in France. These bore oval openings in the calvaria, sometimes of amazing size; and the margins of these openings had become eicatized, showing that the patients had long survived the operations. What is more, the buttons of bone removed from these skulls, and carefully preserved, were found also. Trepanning is known also to have been practised by the prehistoric inhabitants of Peru, and by some tribes of North American Indians, before the age of Columbus. Lucas-Champion-

nière gives here not only a description, with photographic plates, of the most important of these neolithic skulls; but he also argues that the therapeutic effects of decompression, as we know them today, must have been well appreciated by these prehistoric peoples. He compares these facts and specimens with the trepanning practised in modern times by some of the savage or semi-civilized races such as the Kabyles of Northern Africa, the mountaineers of Daghistan and of Montenegro, and in some of the islands of Polynesia.

It is an interesting volume, which forms the first part of a proposed historical study of the operation of trephining; the second part will be welcome when it appears. A. P. C. A.

FURTHER RESEARCHES INTO INDUCED CELL REPRODUCTION AND CANCER. By H. C. Ross. Pp. 63; 5 colored illustrations. Philadelphia and London: P. Blakiston's Son & Company and John Murray.

THE book consists of a ten-page preface by H. C. Ross, in answer to criticisms of his earlier work, and five papers by H. C. Ross, J. W. Cropper, and E. H. Ross. The first paper is a further study of the so-called "auxetics" and "kinetics" described in *Induced Cell Reproduction and Cancer*; the second describes a method for making fixed films of cells studied by Ross' "in vitro" method; the third describes the application of "auxetics" and "kinetics" to cells floating in a fluid medium rather than on a jelly film; the fourth describes an investigation of the gasworks pitch industries and cancer (abridged from the *British Medical Journal*, April 15, 1911); and the fifth describes the action of auxetics on erythrocytes.

What already has been said in reference to *Induced Cell Reproduction and Cancer* (AMER. JOUR. MED. SCI., 1911, cxli, 895) applies equally to the first four of these studies. The fifth paper, by a new worker in this field, E. H. Ross, describes the application of the principles and methods of H. C. Ross to the study of division in mammalian erythrocytes. The author considers the nucleated red cell and granular erythrocyte to be of the same class, but appears to have been more successful in his experiments with the latter cell. The cell may divide into a variable number of daughter cells, depending on the size of the parent cell. Within certain limits, it seems that the further the conditions of the experiment are removed from those of normal adult circulating blood, the more likely is it to be successful.

The book, throughout, shows the same deficiency in detailed report of individual experiments, the same general type of illy founded conclusions, the same disregard of other work in physical biology, and the same diffuse pedantic style of presentation noted in its predecessor.

H. T. K.

COLLECTED PAPERS BY THE STAFF OF ST. MARY'S HOSPITAL, MAYO CLINIC, ROCHESTER, MINNESOTA, 1911. Pp. 603; 250 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

THERE are twenty-three contributors to this volume, of which Mrs. M. H. Mellish is the capable editor. Nearly two hundred pages are occupied by papers dealing with the surgery of the alimentary canal, including nearly every subject of importance from carcinoma of the lips and tumors of the vomer to intestinal parasites and diverticulitis of the rectum. It is rather stretching a point, however, to include "Hodgkin's Disease" and "Sarcoma of the Cervical Glands" among lesions of the alimentary tract. Genito-urinary subjects occupy more than two hundred pages; and it is again somewhat of a shock to find carcinoma of the breast classed here with surgery of the prostate, ureteral calculi, and tuberculosis of the kidneys. The temptation even for abdominal surgeons to have their say on the burning question of the day—the operative treatment of fractures—proves too strong to resist, and we find two papers dealing with this subject. The results secured do not appear to have been particularly brilliant. It is interesting to be told that Mr. Lane employs wooden screws to hold his steel plates in position. Perhaps we may expect in next year's volume accounts of arthroplasties, if not indeed disquisitions on the pathology and treatment of congenital dislocations. "Nil intentatum nostri liquere poetæ."

A. P. C. A.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

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AND

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The Wassermann Reaction in the Rabbit.—In 1908 Sachs and Altmann found that syphilitic sera, which gave a negative Wassermann reaction in the inactivated state, frequently exhibited a strongly positive reaction when active. The fact that certain normal sera also reacted positively prevented the utilization of this fact in a diagnostic way. L. HALBERSTAEDTER (*Berlin. klin. Woch.*, 1912, xlix, 594) has made the interesting observation that the conditions are exactly reversed in the rabbit. He finds that the serum of most normal rabbits, when inactivated, gives the Wassermann reaction. In the fresh, active state, the sera of normal rabbits give a negative reaction almost without exception. Occasionally there is slight inhibition of hemolysis, but never a well marked positive reaction. The serum of rabbits infected with dourine, however, gives a positive reaction. The possibility is, therefore, apparently present of finding specific immunity reactions in the rabbit through the examination of sera in the active state. The observations appear to be of considerable importance in view of the extensive experimental researches, which are being made at the present time on lues.

The Histological Disappearance of Skin Syphilides under Salvarsan.—ROHRBACH (*Münch. med. Woch.*, 1912, lix, 967) has made histological studies of various skin lesions of syphilis under the influence of treatment, particularly with salvarsan. He finds that the specific infiltrations persist for some time, though the diffuse leukocytic infiltrations disappear more rapidly. The morphological picture and the extent of the plasma cell infiltration furnish a good indication as to the more

or less successful destruction of the spirochetes. The early institution of treatment and the administration of salvarsan at frequent intervals markedly influence the quality and rapidity of disappearance of the infiltrations. Endarteritic changes are strikingly affected by treatment. Following salvarsan, the elastic fibers undergo further injury, and may disappear entirely; in other words, elastic tissue is less affected by the living spirochetes than by their endotoxins. In view of the long duration of the infiltrations in many cases, it would appear to be rational treatment to combine inunctions with the salvarsan.

The Histological Structure of Syphilitic Lesions in the Rabbit.—UHLENHUTH, P. MULZER, and M. KOCH (*Deutsch. med. Woch.*, 1912, xxxviii, 1079) have made a histological study of the lesions in syphilitic rabbits. They summarize their findings as follows: Regardless of the source of the material, the nature of the lesions produced is practically identical. There are formed granulations or granulation tumors arising from the mononuclear lymphoid cells; in the central zone there appears very early a tissue suggesting embryonic connective tissue, which the authors designate mucinous degenerated connective tissue. The lymphoid infiltration is usually diffuse, less often in the form of a nodule; in the latter epithelioid cells may be found. Among the lymphoid cells numerous plasma cells are found, and also eosinophile cells. In certain instances plasma cells were so abundant that they predominated. Giant cells were observed in only one case; they were situated in the mucinous degenerated connective tissue. They were quite small and corresponded to the so-called Langhans type. Miliary foci of necrosis, such as are found in the liver and adrenals of newborn infants, were seen frequently, usually in the mucinous degenerated connective tissue. Perivascular lymphoid infiltrations were not uncommon, whereas partial or complete obliteration of the vessels was noted only a few times. In some cases cells filled with fat droplets were numerous at the edge of the lymphoid infiltration next to the mucinous degenerated tissue. The disappearance of the testicular canaliculi was analogous to the condition observed in human syphilitic orchitis, except for the scarcity of elastic tissue fibers in the rabbit. The richness of the lesions in spirochetes is striking and finds its parallel in human congenital syphilis. The lesions in the rabbit resemble those of congenital lues rather than the acquired disease of adults in other respects. There is an absence of extensive necrosis or caseation in the central area of the granulation tumors. The authors consider the mucinous degeneration of the connective tissue seen in the rabbit as a specific reaction of the rabbit—the equivalent of the necrosis or caseation found in human cases.

Recent Modifications of the Romanowsky Stain.—S. SZÉESI (*Deutsch. med. Woch.*, 1912, xxxviii, 1082) reviews some of the more recent modifications of the Romanowsky stain, and concludes that the panoptical method of Pappenheim, which follows, is the best. (a) The dry films are fixed in May-Grunwald's staining solution three minutes. (The stain is a modified Jenner's stain, which is dissolved in methyl alcohol.) (b) Next add an equal quantity of distilled water, and

stain one minute. (c) Pour off the stain without washing, and then treat the specimen with freshly prepared aqueous Giemsa's solution fifteen minutes. (d) Wash thoroughly in water. (e) Blot dry. (Avoid drying over the flame, since the azure staining is injured). (f) Mount in neutral Canada balsam. The erythrocytes are rose colored, polychromatophilic red cells bluish violet, basophilic granulation blue, nuclear particles reddish violet. The nuclei of leukocytes are violet, often reddish violet. The bodies of lymphocytes are light blue, Neutrophilic granules take a brownish color, and are remarkably sharp and distinct. The eosinophilic granules are red, mast cell granules ultramarine blue, azure granules purplish red. The technique is simple, and the results almost uniformly good.

Clinical Experience with Neosalvarsan.—A. STÜHMER (*Deutsch. med. Woch.*, 1912, xxxviii, 983) has had the opportunity of using neosalvarsan in a variety of luetics at various stages of the disease. As with salvarsan, he began by employing intramuscular injections of the drug, but soon abandoned this method of administration for the intravenous route. He finds that neosalvarsan possesses several advantages over the older preparation. (1) The substance is very easily soluble, making the preparation of the solution for administration much simpler. (2) The fact that sodium hydrate is not required in the preparation of the solution eliminates a number of possible dangers. (3) With similar doses, neosalvarsan is better borne than old salvarsan. Intestinal disturbances and collapse are almost never observed. (4) With neosalvarsan the dose may be increased to twice that employed with old salvarsan. Drug rashes are more frequent, but lead to no permanent injury. (5) The activity of the preparation in man certainly equals that of old salvarsan; in animals the new preparation greatly exceeds old salvarsan in potency. (6) Intramuscular injection of neosalvarsan causes much less local irritation, and the absorption is much more rapid than with old salvarsan.

Perpetual Arrhythmia.—H. A. FREUND (*Deutsch. Archiv. f. klin. Med.*, 1912, evi, 1) reports a clinical and pathological study of cases of perpetual arrhythmia. The conclusions he arrives at are as follows: The view that perpetual arrhythmia is due to exclusion of the impulses, which normally arise in the node of Keith and Flack, is supported by Freund's findings, for all cases showed marked anatomical changes in this region. The long-continued arrhythmias probably have their origin in injury to the conduction system. The more severe the injury, the less frequent becomes the pulse. Thus a clinical syndrome may develop, which simulates closely Adams-Stokes' disease. From typical cases of Adams-Stokes' disease, such a case is distinguished by the absence of auricular systoles; the jugular vein shows the ventricular venous pulse. Possibly through severe tissue injury in the auriculoventricular region, attacks of ventricular tachycardia may arise. However, periodic auriculoventricular automatism may be present without serious disease of the auriculoventricular region. If one assumes that auricular fibrillation is the explanation of the perpetual arrhythmia, the cause of the irregularity in ventricular action is clear.

SURGERY

UNDER THE CHARGE OF

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The Treatment of Nevi, Based on More than 2000 Cases.—BUNCH (*British Med. Jour.*, August 10, 1912, 296) says that during the last two years and a half he has treated over 2000 nevi by solid carbon dioxide, apart from other skin diseases. For stellate, capillary, cavernous, and flat pigmented nevi the method is excellent, and gives most satisfactory results. For linear nevus, and nevus verrucosus, where there is much thickening and warty growth, it is not so good, but these cases are, of course, very rare. For port-wine stains (*taches de feu*) it depends how far the corium and underlying structures are involved; the most satisfactory cases are port-wine stains with a nodular, irregular surface, and warty projections, and for these there is no other really satisfactory method of treatment. But for the vast majority of nevi there is no more effective treatment, satisfactory, and painless remedy, nor one which gives such uniformly good results.

A Study of Sprain Fracture as an Essential to the Occurrence of Dislocation.—ROSS (*Annals of Surgery*, 1912, lvi, 599) made a study of this subject from experimental work on lower animals, and the cadaver and from x-ray observations. He concludes that practically all, if not all, dislocations are permitted by the primary occurrence of strain of tendons and ligaments, followed by avulsion of tendons and then sprain-fracture, or gross fracture. It is possible that some dislocations are permitted to occur by separation of the fibres of the capsule in place of by sprain-fracture or gross fracture. All dislocations should be skiagraphed, and if evidence of fracture is not found at first, pictures should be taken in many planes. All dislocations should be treated as if fracture had occurred, even in the event of negative x-ray evidence. Some sprain fractures are too small to be shown by x-ray pictures. Often there is spontaneous reduction of dislocations, and sprain-fractures or gross fracture is the only evidence left that can be detected by the x-rays. The sites of sprain-fractures or gross fractures provide the foci from which the osteoblasts issue, in those cases showing excessive callus or covering of joint surfaces with osseous tissue; moreover, the softer tissues found in joint cavities within a short time after the occurrence of dislocations are often in some stage of transformation into bony tissue. Sprain-fracture

or fractures occurring consistently in experimental dislocations on cadavers afford the most positive proof of the fact that dislocations are permitted to occur in this way; but failure to demonstrate sprain-fractures or fractures consistently in experimental dislocations on cadavers means nothing, since the stage to which degeneration has advanced determines whether the greater tensile strength remains in the tendons and ligaments or not. Whether the force be suddenly or slowly applied, sprain-fracture or fracture precedes the occurrence of practically all, if not all, dislocations.

Operation for Pneumatocele of the Parotid Gland and Stenson's Duct (Glass-blower's Tumor).—NARATH (*Deutsch. Zeitsch. f. Chir.*, 1912, cxix, 201) says that pneumatocele of the parotid gland and Stenson's duct gets little attention in the text-books. He reports a case which he believes is the only one to be reported up to the present time in which the condition was cured by operation. His patient had a swelling of the right cheek which had developed slowly from glass blowing, during a period of about nine years. He did not give up his work, and in 1901, about a year before Narath saw him, the inflammation extended to the mouth and increased rapidly, so that he was compelled to discontinue his work. He was admitted to Narath's clinic, November 10, 1902. On examination the orifice of Stenson's duct on the right side was distinctly larger than on the left, and the surrounding tissues were red. By pressure on the right cheek a thin fluid and air appeared. Both cheeks were rather lax, and on the left side the parotid was better defined than on the right. On blowing out his cheeks, as in his work, they became much distended, and presented a globular projection. On the right side there appeared suddenly in the region of Stenson's duct and the parotid gland, a tumor about the size of the thumb below the zygoma and opposite the lobule of the ear. When the patient stopped blowing out his cheeks, the tumor remained stationary. When it was pressed upon by the finger, it disappeared with a sound somewhat like that in an incarcerated hernia on reduction by taxis and the patient had the feeling of air and fluid entering the mouth. Stenson's duct could easily be located and probed. After the failure of conservative methods of treatment, an operation was proposed to the patient and accepted, the object of which was to reestablish the valve mechanism at the orifice of the duct in the mouth, which was now insufficient. The peripheral half of the duct was exposed by an incision parallel to the duct, and was found to be represented by a loose sac which was easily isolated. It was ligated close to its orifice in the mouth, and divided internal to the ligature, so that the latter remained attached to the portion of the duct continuous with the gland. From the wound a probe was bored obliquely through the cheek muscles until its end made the mucous membrane of the mouth prominent. An incision was then made over the end of the probe which was passed into the mouth. The ligature attached to the free end of the duct was tied to the outside end of the probe, and the duct thus drawn into the mouth through the passageway made by the probe. To make a better valvular closure the duct was twisted slightly on its axis and sutured to the margins of the opening in the mucosa so that its end projected into the mouth 2 to

3 mm. Healing was good and the gland condition was soon much better. But a second operation became necessary for a threatening stricture at the orifice of the duct, and was performed two months after the first. An incision was made over the duct to the parotid tissue, and the duct isolated. The gland with the duct formed only a sac which was drained externally by a rubber tube through a passage made with a slender forceps behind the lower jaw. In the following weeks an effort was made to destroy the remaining parotid tissue from which only a small quantity of secretion was exuding. One injection of alcohol and three of chloride of zinc accomplished this purpose. The fistula closed two months later, and the patient returned to work as a glass blower seven months after the second operation. He found that he could do his work better than before the operations, and had no further trouble. There resulted little or no disturbance of the facial nerve which is so frequently injured in operations on this gland.

A Contribution to Surgery of the Heart.—WAGNER (*Deutsch. Zeitsch. f. Chir.*, 1912, exix, 221) quotes Erich Hesse as claiming, on the basis of 21 operated cases, that in 50 per cent. of all cases an exact diagnosis of heart wound was impossible. Of 7 cases seen by Wagner and operated upon in the Stettin City Hospital, in which a diagnosis of heart wound had been made before operation, the diagnosis was confirmed by the operation in only 5, and it was found that in 2 the bullet had passed by, close to the heart. A wound within the heart area does not, of necessity, indicate a heart wound, nor does the direction of the bullet always furnish a good guide. In the above 5 cases of heart wound, confirmed by operation, there were no abnormal sounds heard over the heart. Erich Hesse noted such sounds in only 1 of his 21 cases. Wagner observed an increase of the area of heart dulness in only 1 of his cases. Tamponade and strangulation of the heart is the most important symptom when it is present, but Wagner observed it only once in the 5 cases confirmed by operation, and Erich Hesse found it only 8 times in his 21 cases. Frequently the blood escapes from the pericardium through an opening into the pleural cavity. Anemia is usually present, but is not characteristic of heart wounds. The subjective symptoms of precordial distress, pain in the heart region, feeling of pressure and dyspnea, can aid in the diagnosis, but are not positive signs. Early diagnosis, therefore, is beset with difficulty, but is very important for a favorable outcome from operation. It is known that severe heart wounds can be almost symptomless. As the result of his studies, Wagner believes that as soon as a probable diagnosis of heart wound can be made, the heart should be exposed promptly, in civil life, by operation. This rule does not hold in war. He reports a case in which a heart wound was assumed to be present with certainty, and in which operation showed positively that the heart was not wounded. There was hemopericardium and hemothorax, but no wound of the heart. Undoubtedly the patient would have recovered without operation. The probability is that the bullet took a course tangential to the heart, opened the pleura, and passed through the lung. Lundmark reported a case which was very similar to this one.

THERAPEUTICS

UNDER THE CHARGE OF

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The Production of Active and Passive Immunity to the Pneumococcus with a Soluble Vaccine.—HIRSCHFELDER (*Jour. Amer. Med. Assoc.*, 1912, lix, 1373) says that the extensive employment of vaccines made from dead microorganisms has been followed by variable results. It seemed probable to him that these discrepancies might be due to the fact that in the one case an efficient quantity of the bacterial endotoxin has entered into the circulation, whereas, when no beneficial results ensued it might be that a satisfactory extract of the microorganisms had not been obtained. He made an extract by acting on living pneumococci with an alkaline pancreatin solution at 37° C. for a definite time, stopping the action by slight acidulation, and filtering through a Pasteur filter. Rabbits injected with a single dose of the extract developed relative or complete immunity to a virulent pneumococcus culture in about six or seven days. In order to determine whether it would be possible to produce a serum which would afford passive immunity, a dog was injected with increasing doses of the pneumococcus extract. The serum obtained from this dog and injected intravenously into rabbits protected them from fatal inoculations of a virulent culture of pneumococci. Unfortunately, the serum of the dog cannot be used on human beings on account of its toxicity, and experiments are being made for the purpose of producing anti-pneumococcic serum from sheep and horses. Ten patients with pneumonia were treated with the extract, and all recovered. In a majority of the cases the crisis occurred within twenty-four hours after the first dose. A striking fact was a rapid fall of the number of leukocytes within twelve hours and preceding the reduction of temperature. Hirschfelder admits that the number of the cases is far too small to warrant an estimate of the value of the treatment, but he believes that his results certainly prove that the treatment is harmless.

The Duration of Immune Bodies in the Blood after Antityphoid Inoculation.WOLLSTEIN (*Jour. Exper. Med.*, 1912, xvi, 315) found that in a series of 24 persons inoculated with antityphoid vaccine that immune bodies in the blood reached their height within two months after the first inoculation, or one month after the third inoculation, then fell rapidly within the next two months. Only 19 of the cases could be followed longer, and 8 of these were negative for bactericidins within ten months after inoculation, and 15 were negative after thirteen months. Only one serum reacted in a dilution of 1 to 1200 at the end of thirteen months. Wollstein says that there is, of course, no justification for the conclusion that clinical immunity

can be determined absolutely by the measure of immune bodies in the blood, since experience has apparently proved the contrary, a fact which can be accounted for by the latent power of the body cells to react more quickly to a stimulus which has once made them sensitive. That this power lasts for many years after an attack of typhoid fever is well known. Further study is required to prove its duration after antityphoid inoculation. It would seem, however, that reinoculation with typhoid vaccine within a year is indicated when exposure to typhoid fever seems imminent.

The Administration of Salvarsan in Syphilis.—FORDYCE (*Jour. Amer. Med. Assoc.*, 1912, lix, 1231) says that the efficiency of salvarsan bears a direct relation to the age of the infection. In the early stage three or four doses supplemented by mercury will in many cases cure the disease in from six months to a year. The florid stage requires more intensive treatment; five or six doses followed by several mercurial courses are necessary. In some forms of syphilis of the nervous system the effects of salvarsan are more satisfactory than those of mercury and potassium iodide. In malignant syphilis, when mercury has been given over a long period continuously, without changing the clinical manifestations or the blood reaction, not infrequently all of the manifestations disappear after one or two doses of salvarsan. These patients probably develop more or less immunity to mercury, or their strains of spirochetes are more amenable to arsenic treatment. A reaction uninfluenced by a long course of mercury may be changed by one or two injections of salvarsan. In other words, a combination of salvarsan and mercury is more efficient in changing the blood reaction than either alone. In the primary stage it is possible permanently to reverse the blood reaction with salvarsan, but, as the disease grows older, the probabilities of changing it with only a few doses grow less. The introduction into the system of such large quantities of the drug as is possible with neosalvarsan may so concentrate the treatment that all or most of the organisms are destroyed, but it has not yet been used long enough to enable us to draw definite conclusions.

The Effect of Benzol on Leukemia.—KORANYI (*Berlin. klin. Woch.*, 1912, xlix, 1357) reports a typical case of leukemia that improved remarkably apparently as a result of the systematic administration of benzol. The patient was a woman, aged thirty-two years, who noticed seven months before applying for treatment, that her spleen was enlarging, and that she had become very weak. The blood count showed 3,100,000 red blood cells and 220,000 white blood cells, including 70 per cent. polynuclears, and 16 per cent. myelocytes. A single exposure to x-rays was made February 1, 1912, and two weeks later the benzol was commenced, giving from 3 to 4 grams a day. By April the white blood cells had dropped to 65,000, and by the middle of May to 8,000, and the general health showed marked improvement. Koranyi has tried this treatment in a number of cases of leukemia, and as yet there have been no failures. The spleen subsides to normal size in time, but there is less effect upon the lymph nodes. The benefit is more gradual than from x-ray therapy, but the benzol may succeed

in cases where radiation has failed to benefit. Patients who have already had x-ray treatment seem to respond more readily to the action of benzol. Doses of even 5 grams of benzol during the day gave rise to no serious by-effects. The stomach disturbances such as burning in the stomach, eructations, and dizziness may be avoided by giving an equal amount of oil in a capsule together with the benzol. Koranyi's attention was first called to the action of benzol upon the blood by Barker's report of three cases of purpura hemorrhagica with aplastic anemia, in 3 girls who worked with benzol in a factory. Two of these cases ended fatally. Selling's experimental research has further established that benzol first increases the production of leukocytes and then has a destructive action on them, while the number of red blood cells is not modified. At the same time it was observed that the bone marrow, the spleen, and entire lymphatic system showed marked aplasia.

Absorption of Food in Typhoid Fever.—Du Bois (*Arch. Int. Med.*, 1912, x, 177) relates the results obtained by him in a study of the absorption of the high calory diet in typhoid fever as advanced by Coleman. Du Bois found that carbohydrates when given in amounts under 300 grams a day were present in the stools only in traces, if, indeed, they were present at all. When amounts larger than 300 grams were given, the stools sometimes contained 2 or 3 grams of reducing bodies. The nitrogen of the feces averaged 1.12 grams a day, and never exceeded 1.8 grams, amounts which are within normal limits. The loss was 7.1 per cent., which is a figure lower than that of previous observers. This, perhaps, may be due to the fact that the diet was less irritating to the intestinal tract. With the fats there seemed to be a diminution of both the percentage loss and the actual weight of fat in the feces as the disease progressed. Du Bois says it is hard to give averages which are fair, but it can be said that during the first three weeks of the attack and during the height of a relapse, the patients lose on an average 7.2 per cent. of the ingested fat. Later in the disease, with a falling temperature and decreasing toxemia, they lose about 4.5 per cent. The average loss for all cases examined was 6.02 per cent., which, though higher than the normal figure of 3 per cent. for a similar diet, is not enough higher to be of any clinical significance. The dried feces contained from 30 to 50 per cent. fat. However, very large amounts of fat were given. The stools of typhoid patients on the high calory diet resemble normal stools very closely. The indican of the urine, which is rather high during the early part of the disease, decreases steadily as the patient's condition improves. The indican excretion compares favorably with that of Folin's normal individuals. They can absorb very large amounts of fat, but the percentage of absorption is somewhat lower than normal, especially early in the disease.

The Treatment of Leukemia with Benzol.—KIRALYFI (*Wien. klin. Woch.*, 1912, xxv, 1311) reports 7 cases of leukemia treated systematically with benzol. The benzol was given in capsules together with an equal amount of olive oil, each capsule containing 0.5 gram of the drug. The dose at first was four capsules a day, and this dose was

gradually increased until the patients were taking two capsules five times a day. The length of the treatment varied from three weeks to five months. Most of the cases belonged to the myeloid type. The leukocytes returned to normal numbers and the leukemic lesions subsided. The other symptoms of leukemia showed marked benefit from the beginning of treatment. The fever and enlargement of the spleen subsided early in the course of the treatment. In the single case of lymphatic leukemia treated the improvement was noted exceptionally early, the leukocytes dropping to 7200 in three weeks, from 131,200 at first. This case had been treated a year before with the x-rays, with the result of a drop in the leukocytes from 80,000 to 40,000, but an increase in the glandular enlargement. The benzol treatment was also tried in a case of polycythemia with some benefit, but the patient was only under observation a short time. The results in the case suggest that possibly benzol may be of value in regulating blood production in this disease. The author states that the period of observation has been too short to determine whether the benefit will be permanent, but improvement occurred in every case treated.

PEDIATRICS

UNDER THE CHARGE OF

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The Cutaneous Reaction to Tuberculin in Childhood.—C. PAGET LAPAGE (*British Jour. Child. Dis.*, 1912, ix, 493) states that the cutaneous method of von Pirquet is, in children, better, safer, and more reliable than the conjunctival method. The cutaneous test approximates more closely in its results to the subcutaneous, than does the conjunctival. McNeil found better results from undiluted tuberculin rubbed into the unbroken skin than when it was applied as in vaccination. Twenty-five per cent. tuberculin is strong enough to be reliable. The ordinary reaction, occurring within twelve hours, consists of redness and swelling of the area to which the tuberculin was applied, and often involves a larger area surrounding it. Rapid and ephemeral reactions occur within a few hours, reach their maximum in from ten to twelve hours, and disappear in twenty-four to forty-eight hours. Strong, lasting reactions may take two or three days in which to reach their maximum. A delayed reaction does not appear for one or two days. When it does appear it is often well-marked and may last several days or weeks. A reaction indicates that the individual has been infected with the tubercle bacillus. The body may have resisted the disease, and the tubercle bacillus be in a state of inactivity, yet the body will react to the tuberculin. The number of children reacting to the test, increase with their age, although there is probably a diminution after the tenth year. The reaction is increased by tuber-

eulin treatment. It is established that there is no reaction in many cases of advanced tuberculous disease exhibiting cachexia, and in many cases of mixed infection. Slight reactions seem to occur with greater frequency in cases which are negative clinically. Prolonged reactions tend to occur in abdominal or glandular tuberculosis. McNeil claims that the intensity of the reaction varies directly with the vigor of the patient.

Pneumococcal Infection in Infancy and Childhood.—GAVIN FULTON (*Pediatrics*, 1912, xxiv, 599), in discussing pneumococcal infections in childhood reports the treatment of this condition by vaccines. The pneumococcal infection may be general from the start, and the pneumonia a local expression of it. Or the pneumococcus may invade any part of the body and be the primary factor in a local inflammation which may or may not become general. The constitutional symptoms of acute pneumococcal infection are characteristic, irrespective of the seat of the infection. There are chill, high continued fever, tachypnea, increased arterial tension, and evidence of meningeal irritation. A certain proportion of cases of pneumococcal pneumonia do not respond to the routine symptomatic treatment, there being nothing to combat the specific bacterial infection. This fact led Fulton to try out pneumococcus vaccines on a series of cases. These cases received no other treatment except the vaccine and continuous exposure to fresh air. The results in 5 cases detailed by Fulton are very good. The dose was from a half to one bulb of the vaccine containing 40,000,000. The vaccine reduced the temperature, pulse, and respiration within twenty-four hours, hastened resolution, and cut short the course of the disease. In several cases the dose of vaccine was repeated in forty-eight hours when the symptoms again tended to increase in severity, but after the second dose the symptoms became progressively less marked. Most of the cases were of the worst type, with fever of 105° to 107° F., pulse rate from 140 to 150, and respirations from 40 to 60 per minute. The ages were from three months to four and one-half years. One case died. This case was treated in the routine way at first and consent was only procured for using the vaccine after collapse had set in. Fulton believes vaccine to be a legitimate line of treatment, and of value not only in pneumonia, but in pneumococcal infection anywhere in the body. Stock vaccines were used in these cases as the delay and difficulty in preparing autogenous vaccines made this form impracticable.

The Dietetic Treatment of Purulent Affections of the Urinary Tract in Children.—HUGO NOTHMANN (*Berlin. klin. Woch.*, 1912, lxi, 1848) mentions the doubt as to the mode of infection in purulent conditions of the urinary tract in children, and suggests the probability of a hematogenous infection in many cases. Other organisms besides the bacillus coli are presumably causative factors. The latest treatment of these conditions in Germany follows an English method, and is based on the fact that in pyelitis the urine has an acid reaction. Potassium citrate is given during the whole day in large doses. Whether the results are due to the alkaline reaction induced in the urine or to flushing of the urinary tract through the diuretic action, the fact

remains that this treatment gives excellent results in pyelitis with acid urinary reaction in children. In the exhibition of alkaline waters the result is due to the alkalinity induced in the urine. Nothmann found remarkable improvement in cases of pyelitis by feeding a malt soup to the children. This diet is found to render the urine consistently alkaline, while the ordinary milk diets render it acid. Keller's "malzsuppe" was used in these cases. The original formula consists of $\frac{1}{2}$ liter milk, $\frac{2}{3}$ liter water, 100 grams "Loefflund's Malzsuppextract," and 50 grams wheat flour. The presence of calcium carbonate in the malt extract accounts for the alkaline reaction of the urine. Each liter of the above formula contains 1.1 gram of calcium carbonate. This form of feeding, besides improving the urinary condition, greatly improves the general condition and nutrition of the child, and so increases its immunity against the infection. The "malzsuppe" should only be used when the child is old enough to digest this type of nourishment, and where the child's general condition indicates it. Fortunately pyelitis is not so frequent during the first six months of life, so that this form of diet should be applicable to a large number of cases occurring after the sixth month. The "malzsuppe" stimulates appetite, opposes constipation, improves the general nutrition and acts as an excellent therapeutic agent on the purulent condition of the urinary tract.

OBSTETRICS

UNDER THE CHARGE OF

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The Effect of Chloral Hydrate upon the Liver and Kidneys.—HOPKINS, pathologist of the Sloane Hospital for Women, reports (*Amer. Jour. Obstet.*, April, 1912) the results of his studies from the effect produced by chloral hydrate on the liver and kidneys. He finds that occasionally this substance produces fatty changes in the liver similar to those caused by small doses of chloroform. These changes, however, are not identical with those found in eclampsia and in delayed chloroform poisoning. Chloral hydrate produces no histological changes in the kidneys, but causes an increase in the urinary nitrogen, which may be delayed until after recovery from anesthesia, and tends to return again to normal.

Fever in the Newborn.—CAUTLEY (*British Med. Jour.*, May 18, 1912) calls attention to the fact that newborn infants are exposed to septic infection at the umbilicus. Soon after birth they may show the effects of confinement in the various lesions produced by pressure or infection. Changes in the respiratory tract incident to the establishment of respiration and disturbances of digestion, may also cause

fever. The temperature of the newborn is usually depressed by bathing, and short variations in temperature are without significance. The daily rise or persistence of abnormal temperature is important. Fever occurring during the first few days after birth is usually the result of mild toxemia, which disappears with the plentiful administration of colostrum, or of water. In infants born in severe labor, pain and nervous irritation may cause fever, while meningeal hemorrhage usually produces subnormal temperature. Injury to the cranium in labor, followed by meningitis, produces fever, and where the scalp is insufficiently injured to slough, gangrene may develop and septic infection. As a rule, sepsis causes 50 per cent. of fever in the newborn. Of this, 25 per cent. may be ascribed to the digestive tract. Cautley cites the case of a mouth infection, followed by fever and death, and 1 of pustular dermatitis causing severe fever, from which the child gradually recovered. Umbilical sepsis is well recognized as a cause of fever in the newborn. The treatment of the condition consists in preventing infection by antiseptic precautions during labor, by antiseptic dressing of the cord with dry sterile powder, preceded by the application of alcohol. When infection arises chloral is sometimes useful to relieve spasms. For the toxemia, irrigation of the bowels with hot saline fluid is useful, and in severe cases saline fluid should be given beneath the skin. If the bowel movements are offensive, small doses of gray powder are beneficial. Brandy is indicated. So far as the prognosis is concerned, fever following localized infections is not a sign of great danger. Where constitutional symptoms of infection develop, the prognosis is exceedingly grave. Failure to take and to assimilate food, with great depression, are also bad symptoms. Prolonged fever, even with local or general paresis, may often end in complete recovery.

Induced Labor for Pelvic Contraction.—BAGGER-JOERGENSEN (*Archiv mensuelle l'Obstétrique*, February, 1912) reports 29 cases of induced labor in 6400 confinements, among whom were 100 cases of contracted pelvis. In 25, labor was begun by the introduction of a bougie; in 4 by rupturing the membranes. The thirty-fifth or thirty-sixth week of gestation was the time selected. There was no maternal mortality. The morbidity rate was 3.5 per cent. Of the 30 children, 27 were born living, with an immediate mortality of 10 per cent. The secondary mortality during the first year was 8 per cent.

Cleidotomy.—LEIBICH (*Zentralbl. f. Gynäk.*, 1912, No. 19) reports the case of a primipara brought to the hospital in labor with a large child, the mother having a normal pelvis. A general practitioner had applied forceps unsuccessfully, and in his efforts to deliver had lacerated the perineum. The head had not rotated normally and the shoulders had become impacted at the pelvic brim. The forceps had brought the head to the vulva but could not deliver. The position of the child was the second. To dislodge the shoulders cleidotomy was performed from the left side, the arm brought down, and delivery readily effected. The dead child was a male, 55 cm. long, and weighing 5050 grams. The bisacromial diameter was 14 cm., and the shoulder circumference 45 cm. The cleidotomy reduced the bisacromial

diameter to 10.5 cm. and the circumference of the shoulders to 40 cm. Examination of the body of the child showed that the subclavicular bloodvessels had not been wounded. A second case is reported in which the operation was done upon an anencephalic fetus with impaction of the shoulders. Both clavicles were severed and delivery effected by inserting a blunt hook into the right axilla. The reviewer believes that cleidotomy is often neglected in performing difficult vaginal delivery. Where the fetus is dead or dying the obstetrician should refrain from difficult extraction until he has lessened the size of the fetus. His first impulse is to perform craniotomy, but this is often not sufficient, and cleidotomy should be added. The reviewer has several times succeeded by cleidotomy followed by the application of the blunt hook in the axilla, in delivering large dead children with very little injury to the mother.

GYNECOLOGY

UNDER THE CHARGE OF

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Menorrhagia of Puberty.—WEIL (*Ann. de Méd. et Chir. Infantiles*, 1912, xvi, 553) says that cases of very profuse and prolonged uterine hemorrhages, occurring either coincidently with the onset of puberty, or shortly afterward, are seen not very infrequently, and have usually been attributed to some local cause, such as uterine or ovarian congestions, inflammations, or other lesions. From a careful study of several such individuals, however, Weil has come to the conclusion that the condition is, in most instances, merely one manifestation of a general dyscrasia. In 9 cases which have come under his observation no genital lesions whatever were to be found. Most of these girls had showed a clearly marked hemophilic tendency during childhood, and in 7 there was an hereditary tendency to the same condition on the maternal side. Examination of blood taken from a vein showed in every instance increased coagulation time, as did the bleeding test of Duke. This is performed by making an incision 2 mm. in length in the lobe of the ear. If the drop of blood which forms is gently removed without wiping every half minute, bleeding should cease, in a normal individual, in from two and one-half to three and one-half minutes, but in all the cases of menorrhagia at puberty this time was increased, in one instance up to one and one-half hours. In several of the cases a history of icteric attacks was present, and in one there was a remarkable family tendency to icterus. In 5 cases developmental anomalies, such as underdevelopment, gigantism, or obesity were noticeable features. Weil considers the basic trouble in all these cases to be probably some functional disturbance of all the glands of internal secretion—thyroid, pituitary, adrenals, ovaries,

etc. He thinks the hemorrhagic tendency is purpuric rather than truly hemophilic in character, as in no instance was there any evidence of paternal inheritance. He warns that these patients should be kept away from the surgeon, and considers the best treatment to be organotherapy, plus the injection of fresh, normal serum, the latter in many instances being the only thing that will stop hemorrhages which may be so severe as to threaten life. Of the various organ preparations he has found thyroid extract, given in small doses, the most satisfactory.

Lactation Associated with Ovarian Carcinoma.—Two instances of this condition are reported by SAENGER (*Monats. f. Geburts. u. Gynäk.*, 1912, xxxvi, 436). The women were aged thirty-five and fifty-five years respectively; in neither was pregnancy present. Both had showed the presence of distinct lactation before death, and at autopsy the breasts showed the histological picture of functioning organs. In one patient a primary ovarian tumor, presumably a carcinoma, had been removed seven months before death; at autopsy a condition of general carcinomatosis was found. In the second case the uterus, one ovary, and a portion of the other had been removed three years previously; autopsy showed the presence of extensive medullary carcinoma of the stomach with numerous metastases, the remaining portion of the one ovary was completely carcinomatous, and there was an adenoma of the hypophysis. Saenger calls attention to the fact that while the development of the breasts before the occurrence of pregnancy has been shown pretty conclusively to be dependent upon the presence of healthy ovaries, the relations between these structures during pregnancy are by no means so constant, nor are the causes of the not infrequently observed phenomenon of extra-gestational milk secretion thoroughly understood. Such instances have been described in connection with ovarian cysts, and other ovarian tumors, but, so far as he could determine, not in connection with carcinomas. It is well known that occasionally lactation appears after double oöphorectomy, and cases are on record where normal lactation followed castration during pregnancy, so that the presence of the ovaries cannot be considered necessary to its occurrence. In the 2 cases reported by Saenger, however, castration cannot have been the only factor, as in one a portion of one ovary was not removed. Saenger considers the presence of the developing tumor to have been the underlying cause of the lactation in these instances, accepting the theory of Askanazy that embryonal tumors, such as teratomas, can have a specific action on the genital sphere, and that other tumors with but slightly differentiated, embryonic cells—anaplastic carcinomas and sarcomas—can exercise a similar stimulus to hyperplasia of certain organs. Saenger believes that carcinomas developing in the ovary may be especially embryonic in character, and that the unripeness of the tumor, rather than its seat in the ovary, is responsible for its ability to cause changes in distant organs—changes which have manifested themselves not only by the assumption of physiological activity on the part of the breasts, but, in one instance, by the adenomatous proliferation of the hypophysis as well.

Lactic Acid Therapy in Gynecology.—POULIOT (*Rev. prat. d'Obst. et de Gyn.*, 1912, xx, 257) says that while the internal use of lactic acid bacilli is falling off somewhat since the first burst of enthusiasm, the value of these organisms under certain conditions for external application is just beginning to be realized. Lactic acid cultures are not of much use in combatting acute suppurative conditions, but in infections by members of the colon group, by most of the anaërobcs, and especially by the organisms of putrefaction, their antagonistic properties may be utilized to great advantage. For local application liquid cultures are, of course, the best, next to these the powdered "lactobacilline." The compressed tablets Pouliot believes to be often inert, as they may be rendered sterile by the heat engendered during compression. While the use of this form of therapy in gynecology is of distinctly limited application, Pouliot has found it of decided value in the treatment of suitable conditions. He gives vaginal injections of the liquid culture in cases of ulcerated neoplasms of the cervix, necrotic polyps, esthiomène vulvæ, vaginismus (which he considers to be always accompanied by an ulceration, or at least a fissure of the vestibule), and after vaginal hysterectomy by the clamp method, to combat the fetid discharge which always results from necrosis of the pedicles.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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On Ocular Palsies Occurring as the Sole or Most Conspicuous Evidence of Disease.—HAWTHORNE (*Ophthalmoscope*, November, 1911, p. 750) discusses the important question whether in a given case of palsy of ocular muscles, the condition may be regarded as simply a local matter, or whether it is an indication, perhaps the first, of progressive and serious disease of the central nervous system. Probability there may be, one way or the other, but not certainty, or at least certainty only arrives when, through the lapse of time, it is seen that the paralysis was a mere isolated event in the patient's clinical history, or that, on the contrary, it was the forerunner of even more serious mischief. Analogously to disturbances of other peripheral nerves, for example, the facial, palsies of one or more of the ocular muscles may undoubtedly be a purely local phenomenon. The difficult is to be sure that this is the explanation in any individual case. All that can be said, perhaps, in the way of help in this difficulty is, that if the absence of syphilis can be guaranteed, if there are no

other signs of nervous disease, and if the patient is more or less definitely "rheumatic," it is a reasonable conclusion for practical purposes that the paralysis is of the simple order. Not that this necessarily means that it is to be of brief duration or that a complete cure is certain; on the contrary some of the ocular paralyses associated with central organic disease are but slight in degree and transitory in duration. One remark in reference to the simple or rheumatic paralyses may be added: It is that for the most part such paralyses are confined either to a single nerve or to a single branch, or possibly neighboring branches, of one and the same nerve. This rule is not absolute, but it has a fairly commanding range. Of ocular paralyses connected with chronic degenerative nervous disease the relation with tabes dorsalis is of great importance, not only because such paralyses may accompany the other symptoms of the affection, but from the fact that the ocular disturbance may be the first, and for some time the only evidence of those degenerative changes in the nervous system, which in their complete expansion produce the clinical picture of tabes dorsalis. And what is true of tabes is almost equally applicable to its near relation—general paralysis of the insane. Another nervous disease, of which ocular paralysis may be the first symptom, is disseminated sclerosis. Syringomyelia may also include an ocular paralysis among its symptoms, and so occasionally may chronic bulbar disease. In gross intracranial lesions ocular palsies not infrequently occur, but here for the most part there are other and equally conspicuous symptoms. Among intracranial lesions capable of producing ocular palsies may be mentioned polio-encephalitis superior. Chlorosis and otitis media are also occasionally accompanied by paralysis of the sixth cranial nerve. In both of which diseases double optic neuritis may also be present. The important point clinically, is to appreciate the fact that even so terrifying a combination as an ocular paralysis with double optic neuritis does not necessarily mean serious intracranial disease and a correspondingly anxious prognosis.

Pathogenesis of Glaucoma.—FRICKER (*Klin. Monatsbl. f. Augenheilk.*, June, 1912, p. 723) has examined 30 cases of glaucoma (mostly glaucoma simplex) with reference to the blood pressure. This was usually determined by the method of von Recklinghausen, occasionally by that of Riva-Rocci and thence converted to the von Recklinghausen values. Of these 30 cases, 20 males and 10 females, in 4 the heart, bloodvessels, lungs, and kidneys were healthy; 1 had tabes. In these 4 cases the average pressure was 150 (von Recklinghausen), that is, the highest limit in health. In 3 cases, aside from an exceptionally high blood pressure averaging 210 (v. R.), no definite pathological condition was found, although the excessive pressure rendered probable the presence of some obstacle to the circulation. Arteriosclerosis alone was present in 10 cases averaging 195 (v. R.) pressure; of these, 5 showed dilatation of the left heart upon the radiograph and 3 a widened shadow of the trunk of the aorta. Death took place in 2 of these cases, with symptoms of cardiac insufficiency. Arteriosclerosis and interstitial nephritis, with tension averaging 205 (v. R.), was found in 6 cases. Arteriosclerosis and emphysema with tension 185 (v. R.) was observed in 3 cases, and emphysema alone, tension 180 (v. R.),

in 3. Arteriosclerosis with myocarditis, tension 150 (v. R.), was found in 1 case. The great preponderance of arteriosclerosis alone or in combination with lesions of the heart, lung, or kidneys is very striking in this series. If the case with tabes be excepted, no other disease was present; while arteriosclerosis cannot be assumed to be the sole cause of glaucoma, it should be carefully searched for in every case, and if found, the proper treatment should receive serious consideration.

Voluntary Nystagmus.—ELLIOT (*Ophthalmoscope*, February, 1912, p. 70) observed in a healthy young man with normal vision the ability to produce voluntary nystagmus; to do so, the subject stares straight in front of him, and within a second or two the phenomenon begins. It is a binocular horizontal oscillatory movement; the amplitude is large, and the movements too rapid to count. The oscillations cease when the effort is relaxed. There is a feeling of weariness and lateral distortion of the objects during the movements. Of recent years the nystagmus has commenced spontaneously on several occasions, but has been readily controllable.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Hypogenetic Nephritis.—JIANU and MELLER (*Cent. f. allg. Path. u. path. Anat.*, September 15, 1912) detail a case of what has been called hypogenetic nephritis, a term instituted by Babes to describe nephritis in a hypoplastic kidney. A considerable number of cases has been shown, the clinical characteristics being a rapid nephritis of two or three days' duration, with uremic manifestations in a patient attacked by some relatively mild disease, such as bronchitis or influenza. Jianu and Meller's case is characteristic, showing a man, aged twenty-five years, who suffered from a diarrheic attack and died in uremic coma. The kidneys weighed 50 and 55 grams respectively, and were lax and soft; considerable uniform fibrosis and relative diminution of glomeruli were observed, while the moderately damaged tubules showed signs of attempts at regeneration. Such kidneys are from the first insufficient, and suffice only for the daily needs of the body under normal conditions; when there is laid upon them the necessity to excrete in addition even mild toxins, they prove inadequate, are damaged, and the body enters into a state of toxemia so great and so cumulative as to cause death. This toxemia, or the agents which cause it, is responsible for the inflammatory changes that are to be

seen. Such a case could present only academic interest to the practitioner were it not for the fact that the subject, in common with the other reported cases, showed other abnormalities in the direction of hypoplasia; these are oftenest in the formation of the genitalia, and Jianu and Meller deduce the conclusion that the presence of hypoplastic abnormality of the genitalia should forewarn the physician of the possibility of the existence of incompetent kidneys.

Tumors in Cold-blooded Animals.—PLEHU (*Wien. klin. Woch.*, 1912, No. 19) reviews the subject of tumor formation in cold-blooded animals, pointing out that as in the warm-blooded, different forms of carcinoma and sarcoma are found, as well as other forms of neoplasm, the nervous system as yet being the only set of organs that has not been found implicated. Carcinoma is essentially a disease of the old, while sarcoma, a much rarer form of tumor, is not so. Metastasia is infrequent, and this especially so in the case of sarcoma. Plehu considers the erratic growth of cells in the *anlagen* of embryonic organs as the most frequent site of neoplastic growth, but gives instances also of its development in scars. As a causative agent, parasites are not to be considered, although their ability to cause hyperplastic overgrowth is undeniable, a distinction which appears to the reader to be insufficiently proved.

A New Recorder in Wireless Telegraphy.—CH. LEFEUVRE (*Jour. de Physiol. et de Path. gén.*, September, 1912, xiv, No. 5) publishes a strange addition to the literature of wireless telegraphy by showing that he has transcribed, in terms of the longer and shorter muscular movements of the nerve-muscle preparation in the frog, messages sent out from the Eiffel tower at certain fixed times. The spools of a telephonic receiver are used, and currents are induced in the nerve-muscle. The simple apparatus required is shown, as well as the tracings, which indicate by long and short contractions the dashes and dots of the Morse alphabet. The experiments were made at Rennes, about 180 miles from Paris. This strange thing shows the extreme sensibility of the nerve-muscle preparation as a galvanoscope; and it is worth noting that, despite many attempts, no one has yet succeeded in making a satisfactory apparatus for graphic reproduction of the messages received by wireless, such being still taken by sound in telephonic instruments.

Changes in the Liver after Parathyroidectomy.—MOREL and RATHERY (*Jour. de Physiol. et de Path. gén.*, September, 1912, xiv, No. 5) describe with greater certainty than has yet been done the hepatic lesions that follow parathyroidectomy, which they find constantly present. The intensity of these lesions does not depend on the time that elapses after the removal of the parathyroids, and the simultaneous removal of thyroid tissue does not affect them; hemorrhages in the liver are not marked, nor do they occur with constancy, and the amount of fat in degenerated areas, depending upon the alimentation of the animal, varies widely. The cellular changes observed consist of the appearance of areas of homogeneous degeneration of the protoplasm, modifications in number and form of the fuchsin-staining granules, fragmentation and granule formation in the protoplasm, and

on one occasion, cytotoxicity. These marks of acidosis were practically reproduced by the intravenous injection of less than fatal amounts of ammonium carbonate.

Comparative Toxicity of Methyl and Ethyl Alcohol.—The occurrence of large numbers of fatal cases of methyl alcohol poisoning gives interest to the experiments of NICLOUX and PLACET (*Jour. de Phys. et de Path. gén.*, September, 1912, xiv, No. 5), with regard to its toxicity in comparison with ethyl alcohol. In a single large dose given intravenously methyl alcohol is the less toxic, but at death there is a greater proportion found in the blood and the tissues; of the tissues, the brain is the most avid in fixing either form of alcohol. If the alcohol be ingested and in repeated doses, methyl alcohol is the more toxic, because it is capable of less complete combustion, and is eliminated more slowly; a quarter of the methyl alcohol ingested is found in the excretions and the excretory organs. In spite of these facts, Nicloux and Placet consider that it is necessary to invoke the impurities of methyl alcohol to explain the numerous fatal cases unless it can be proved that man has a particular susceptibility to the action of the drug.

The Lesion in Whooping Cough.—MALLORY and HORNOR (*Jour. Med. Research*, November, 1912, xxvii, No. 2) were fortunate enough to obtain material from 3 cases dying of whooping cough, and to be able to observe the lesions in the trachea and the bronchi. The bacillus which they found is probably identical with that described by Bordet and Gengou, and the chief interest of their observations lies in the fact that the bacteria are found in large numbers between the cilia of the epithelial cells, lying thus on the surface. The cilia are interfered with and perhaps even destroyed; the normal removal of secretion is prevented and the respiratory surface kept continuously irritated, so that cough is produced. The toxic effects of the bacillus, while undeniable, are, nevertheless, relatively unimportant.

The Serum Diagnosis of Echinococcus Infection.—B. HAHN (*Münch. med. Woch.*, 1912, No. 27) has conducted experiments in the serum diagnosis of echinococcus according to the complement-fixation method of Ghedini, and considers it an effective method for infection by *Tænia echinococcus* or *Tænia saginata*, although he admits that now and then a definitely infected case shows a negative result. The most effective antigen is watery bladder-washing, freshly used. Watery extract of echinococcus or of *saginata* is utilized. Notwithstanding this scientific advance, it is likely that the visual method will remain the favorite means of diagnosis for some time to come.

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THE
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ORIGINAL ARTICLES

SOME OF THE DISPUTED PROBLEMS ASSOCIATED WITH
SURGERY OF THE LARGE INTESTINE.

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MUCH can be learned concerning the underlying causes of diseases of the large intestine by studying the changes which have been incident to the development of its function. In the adult human the large intestine appears as a continuous whole, yet functionally it is sharply delimited at the point of vascular anastomosis between the derivatives of the superior and inferior mesenteric vessels at the splenic flexure. The first half of the large intestine is derived from the same embryologic sources as is the small intestine, and has a similar important metabolic function. About 50 per cent. of the fluids and 10 per cent. of the solids are absorbed in this part of the large intestine. Beyond the splenic flexure absorption is limited in amount, the bulk of absorbable material placed in the rectum being promptly passed into the proximal colon for absorption.

It has been shown by Bond,¹ Cannon,² and others that there is a fairly constant antiperistalsis in the large intestine which passes material back toward the cecum.

The study of comparative anatomy in the herbivorous demonstrates the enormous absorptive value of the cecum. Lyle³ has aptly compared its storage function to the stomach. Unlike the stomach which absorbs but a small amount, the cecum absorbs actively. In some animals there is a sphincter in the ascending

¹ Med. Rec., August 12, 1905, 246-252.

² British Med. Jour., 1906, ii, 238.

³ Amer. Jour. Phys., 1898, i, 359.

colon to hold the material in the cecum. In man a marked physiological activity is shown at this point, although no colic sphincter exists.

The portion of the duodenum which lies between the pylorus and the opening of the common duct may be said to be the vestibule of the small intestine, the food passing rapidly through to reach the area of absorption. In a general way the same conditions exist in the descending colon, which also acts as a vestibule through which food refuse passes rapidly to reach the storage chamber of the sigmoid. The splenic flexure of the colon is held high, as a mechanical means of maintaining food products as long as possible in the first half of the large intestine. This method of retention is more economic in its operation than a muscular sphincter apparatus would be. Some sixty years ago Rokitsky⁴ called attention to the fact that the descending colon was usually found empty at autopsy, just as the x-ray bismuth picture today so often shows it in the living, and which is so often misinterpreted as evidences of supposed stricture.

In an article written in 1900⁵ I called attention to a contraction of the ileocecal orifice as a cause of certain intestinal phenomena, and pointed out that many cases of constipation might have their origin in metabolic changes in the small intestine rather than in the large. This helps to explain the obstinate constipation which sometimes continues after an ileosigmoidostomy, although such stasis is largely due to the fact that the material from the ileum as it enters the sigmoid passes backward by an antiperistalsis into the first half of the large intestine and then pursues its ordinary course much as though ileosigmoidostomy had not been done. This has been demonstrated in the x-ray findings following ileosigmoidoscopy in some of our cases.

The sigmoid varies greatly in its length, size, and position because it is a late development without fixed characteristics (Finney⁶). This is further shown in the weakness of its walls, which in the middle and later decades of life so frequently permit hernias of the mucosa through the musculature. These hernias or diverticula are an important factor in the causation of localized peritonitis from diverticulitis, as well as occasionally the chronic irritating focus in initiating cancer of the sigmoid.

The rectosigmoid juncture is at the third sacral vertebra, and here nature has again introduced certain mechanical obstacles to prevent the too ready discharge from the storehouse of the sigmoid into the rectum. So often a well-trained nurse asks, "Shall I give a high injection with the colonic tube into the colon or a low rectal?" The result, of course, is quite the same. The colonic

⁴ Handbuch der spec. path. Anat., 1842.

⁵ Mayo, Annals of Surgery, September, 1900.

⁶ Trans. Amer. Surg. Assoc., 1908, xxvi, 475-516.

tube pushed through the anus out of sight lies coiled in the rectum when it is supposed to be in the colon. Such a tube cannot often be made to pass through the rectosigmoid in this manner.

The rectum is not normally a fecal storehouse, although through habit it often becomes so, especially in the female. Examination of the male for service in the army shows the rectum to be empty normally.

Bands of adhesions are often developed during adult life. At the time of birth the cavity of the omentum is obliterated as high as the transverse colon. The process continues until in adult life points of adhesion are found as high as the pyloric end of the stomach, which obliterate the lesser cavity of the peritoneum to a greater or less degree. Similar conditions may exist between the omenta and the gall-bladder, and may be taken as evidence of infection. Various observers have asserted that the adhesions which sometimes exist between the epiploic tags of the sigmoid and the abdominal wall, etc., are of great importance, and always the result of pathological conditions; yet such adhesions will be found in a certain percentage of necropsies on subjects over forty years of age, who during life showed no symptoms ascribable thereto.

Jackson⁷ has called attention to the veil of adhesions so often present between the ascending colon and the abdominal wall as a cause of pathological symptoms. We can at least say safely that this condition, like the others mentioned, is developmental in origin. The cecum does not reach its normal situation until about the time of birth, therefore the attachment between this late arrival and its fixed place of abode is recent, and resembles adhesions of a peculiar pannus type. The weakness of this attachment on the right side is partially instrumental in permitting the prolapse of the cecum into the pelvis. Wilms⁸ believes this prolapse to be of great pathological significance in producing cecal stasis. "Lane's kink" is undoubtedly also of developmental origin, and due to a fixation by bands of the terminal three inches of the ileum. The important question is, Do these conditions produce symptoms, or are they merely anatomical deviations without pathological meaning?

The transverse colon averages in length from 20 to 22 inches, and has 10 or 11 inches distance to travel from the hepatic to the splenic flexures. Its supporting attachments in the centre are to the movable stomach, therefore prolapsus of the transverse colon is common. There is little else it can do. The length of the transverse colon serves a physiological purpose in picking up the final remnants of nutritive material. The x-ray photograph taken with the patient in the standing position, with the weight of the bismuth in the stomach or in the transverse colon, or both, pro-

⁷ Surg., Gyn., and Obst., 1909, ix, 278-287.

⁸ Arch. d. klin. Chir., 1903, lxxix, 795-842.

duces an exaggeration of this normal condition. How often can we say that it is truly pathological?

If the small bands of adhesions which are found in one case, such as a sigmoidepiploic tag attachment to the abdominal wall, be productive of so much harm in one patient, how can we expect that another patient with similar symptoms will be benefited by the bands of adhesions which the surgeon purposefully forms to hold up a prolapsed organ like the cecum? How much of truth and how much of fancy is embodied in the elucidation of this subject no one can say. That it is most obscure we all agree. One group of observers is convinced that the whole thing is mechanical and the result of some type of infection rather than an error of development. Another group contents itself with the belief that these patients are all neurasthenics, although they are less ready to give an opinion as to the cause or nature of the condition. That many of the patients operated on have been greatly benefited cannot be denied, yet if one were to take the case histories and reports of successful treatment by means of such mechanical therapy and put them all in a hat to be picked out at random, one could not determine from the histories of the patients those who had been relieved of symptoms by operating for a mobile cecum, for relief of the adhesions, for mobility of the sigmoid, for fixation of the sigmoid, for prolapse of the stomach, and, for that matter, for movable kidney. The histories read alike, but the operations seem to vary with the bias of the operator. Are all of these deductions wrong? Have the profession in regular medicine with their accurate observations no conclusions which depend upon more authentic data? To say that relief of symptoms demonstrates the truth of the opinion is not sufficient unless we grant the same privilege to the mental healers.

I think we can agree with Arbuthnot Lane that metabolic changes may take place in the large intestine, which in some cases produce symptoms of disease and that absorbable toxic products are responsible for many of the symptoms which are spoken of in a general way as gastro-intestinal neurosis, intestinal toxemia, intestinal stasis, putrefactive intoxication, etc.

It is probable that the first part of the colon, and especially the cecum and ascending colon, will be found at fault. To it is delegated the difficult function of culling out the last nutritive remnants from the now infected mass of food. Carcinoma of the cecum and ascending colon are often accompanied by the most profound anemia in cases without glandular or general metastasis. We not infrequently see a removable tumor and a perfect cure follow an operation upon a patient so anemic that the hemoglobin runs as low as 30 and the reds in the vicinity of 2,500,000. Many such patients have been left to die because this specific anemia was believed to be a cachexia from hopeless malignant metastasis.

This same anemia may accompany tuberculous tumor of the cecum of the hypertrophic variety without ulceration to explain it, but is not found to accompany tumors of the sigmoid even though there may be sloughing.

It is possible that all of these mechanical conditions have some effect in detaining the infected remnants of food too long in the absorbing half of the colon, the symptoms being due to the effect of the toxic products absorbed on the controlling sympathetic ganglia. That the theory of mechanical causation alone is insufficient explanation is established by the fact that, as a rule, none of the ordinary results of mechanical obstruction exist, such as muscular hypertrophy of the wall of the bowel, etc. Quite the opposite condition exists—the bowel is thin walled and ballooned, the patients showing marked evidence of loss of sympathetic balance of the neurasthenic type, resembling in some respects a mild Graves' disease from hyperthyroidism.

The views of Arbuthnot Lane,⁹ Rovsing,¹⁰ Coffey,¹¹ Jackson, and others should receive careful consideration. Whether or not the particular operations advocated by these surgeons are ultimately found to be correct, at least their work has called the attention of the profession to an important and heretofore neglected field, and offers a possible explanation of the cause of the protean symptoms in a large group of patients who have received much treatment and little benefit from the medical profession, and who have been exploited by the dietetic fadist and the charlatan.

THE RELATION OF ANAPHYLAXIS TO IMMUNITY AND DISEASE.¹

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STUDIES of the phenomena of protein sensitization, so-called anaphylaxis, have given us quite a new idea of many of the problems of immunity and disease. The only way in which cells of any kind—bacterial, protozoal, or animal—can grow and multiply is by elaborating ferments which split up the pabulum within their reach, thus preparing a food supply. The cell which can no longer supply a digestive ferment is already dead, whatever be the kind

⁹ Surg., Gyn., and Obst., February, 1908, 115.

¹⁰ Samml. klin. Vortr., 1906, xv, No. 431.

¹¹ Annals of Surgery, January, 1907, 43-49.

¹ Read at the Fifteenth International Congress of Hygiene and Demography, September, 1912.

or amount of pabulum surrounding it. The cell which supplies only such ferments as cannot digest the food supply within its reach dies immediately. This is the fundamental fact of the general immunity possessed by higher animals against the lower forms of life. As was shown in my laboratory some years ago, there is no constant and fixed relation between the toxicogenic and pathogenic properties of bacilli. The *Bacillus prodigiosus* contains enough intracellular poison to kill guinea-pigs when injected intraperitoneally in doses of 1 to 90000 body weight, while the anthrax bacillus requires 1 to 1700, and still the former is non-pathogenic and the latter highly pathogenic. The explanation lies in the fact that the *prodigiosus* cannot grow and multiply in the animal body, because its secretions do not digest the proteins of the animal body, or, what is more probable, the secretions of the body cells destroy the bacillus. On the other hand, the anthrax bacillus elaborates ferments which do digest the proteins of the animal body, while the body cells do not destroy the bacillus, and thus serve the microorganism with food. For these same reasons a given bacillus may be pathogenic to one species or to one race and wholly devoid of effect on other animals. Furthermore, the virulence of different strains of the same microorganism varies with the abundance and the strength of the digestive ferment. One strain of the pneumococcus may not kill guinea-pigs in less doses than 1 c.c. of a twenty-four-hour culture, while another may kill in one-millionth of this amount, and still when animals inoculated with the two strains are dead the same number of bacilli or the same amount of bacillary cell substance will be found in both. One strain has multiplied a million times faster than the other, because of the greater abundance and effectiveness of the secretions which enable it to grow.

The great lesson which we have learned from our studies of anaphylaxis is that the digestive secretions of body cells may be developed and modified by the kind of protein brought into contact with them. When a foreign protein is introduced into the animal body certain cells develop a specific digestive ferment which splits up that protein and no other. Cellular digestion is a physiological process and it is normally specific inasmuch as the secretion of each kind of cell splits up the pabulum in such a way as to supply the needs of its own cell, but the pabulum upon which the cells of the body normally feed consists of the proteins of the blood and lymph. From these sources all the cells of the body select their food material through the agency of their digestive ferments. Normally there is much preparation of the foods upon which the cells of the animal body feed. The proteins taken into the alimentary canal are broken up by the digestive juices into amino acids and in this process they lose all their distinctive character. During absorption or soon thereafter the amino acids are put together again, but now so grouped as to form the proteins peculiar to the species.

From the special proteins, thus prepared, each kind of body cell obtains its nutriment. Parenteral digestion is a physiological process in which the material acted upon, the cleavage agents and the assimilating cells are constant. However, even with all this preparation of food for the body cells it must happen at times that foreign proteins, as such, find their way into the blood and lymph. In order to digest this unusual pabulum the body cells elaborate a specific ferment, which digests this protein and no other. This is one of the fundamental and central facts of protein sensitization.

The second fundamental fact in protein sensitization is that every protein molecule contains a poisonous group. This is true of all bacterial, vegetable, and animal proteins so far as they have been investigated. The poisonous group in the protein molecule is the same so far as its physiological action is concerned, whatever be the nature of the entire molecule of which it is a part. Chemically there must be differences in the poisonous groups of different protein molecules, but, as has been stated, in physiological action one cannot be distinguished from another. It may be that more exact studies will show slight variations in physiological effect. I have designated the poisonous as the primary group in the protein molecule. I have also suggested that it be regarded as the "archon" or keystone of the protein molecule. It probably contains the benzol ring with nitrogenous side chains. Attached to this primary group are secondary groups which may be designated as the "characteristic" groups, because it is in these that one protein differs from another. The sensitizing properties of proteins reside in the secondary groups, because it has been shown that these when freed from the poisonous group may sensitize animals to the unbroken molecule. It is for this reason that the special ferments elaborated in the cells of the animal under the influence of a foreign protein are specific. The poisonous group, when detached from its secondary or characteristic groups, does not sensitize either to itself or to the whole protein from which it came. In the original protein molecule the poisonous group is rendered inert physiologically by being combined with the secondary groups. In its free state it becomes a poison on account of the avidity with which it disrupts other protein molecules and combines with their secondary groups. The protein molecule may be compared to a basic or neutral salt, and it becomes more and more poisonous as its basic elements are removed, and when the free acid only is left, its maximum toxic action is reached. The protein poison is a powerful agent. In the purest form in which I have been able to obtain it, and this probably is far from chemical purity, it kills guinea-pigs of from 200 to 300 grams weight, when injected intracardially in doses of 0.5 milligram. When used intra-abdominally this dose must be multiplied by 16, and when given subcutaneously, by about 32. These differences in effect according

to the method of administration are of importance and are accounted for by the fact that the poison attacks and is neutralized by the body proteins with which it first comes in contact.

Whenever neutral proteins undergo cleavage as the result of the activity of proteolytic enzymes, there are steps in the process, when the activity of the poisonous group is made more manifest and this proceeds as the basic elements are stripped off. In this way the poison is in part liberated in alimentary digestion. Biedl and Kraus have shown that the action of the anaphylactic poison and that of pepton are identical. This is necessarily true because the active group in both is the same. The protein poison is set free or activated by the alimentary proteolytic enzymes, and if it were a readily diffusible substance all proteins would be poisonous to man when taken by the mouth. But since it does not speedily pass through the alimentary walls and since additional cleavage renders it inert we escape its poisonous action. In parenteral digestion of proteins there are no walls to prevent the diffusion of the poison, and consequently more or less injury always results.

Anaphylactic shock is such a striking phenomenon that for a long time it obscured the essential facts of protein sensitization and led investigators far astray. When compared with immunity the two seemed antipodal; in one the life of the animal is saved; in the other it is jeopardized and in the majority of instances lost. Indeed, it was a misconception which led Richet to select the term "anaphylaxis." I still hold to the following statements concerning protein sensitization first formulated by Wheeler and myself.²

1. Sensitization consists in developing in the animal a specific proteolytic ferment which acts upon the protein that brings it into existence and on no other.

2. This specific proteolytic ferment stored up in the cells of the animal as a result of the first treatment with the protein remains as a zymogen until activated by a second injection of the same protein.

3. Our conception of the development of a specific zymogen supposes a rearrangement of the atomic groups of the protein molecules of certain cells in the animal body or an alteration of the molecular structure. In other words, we regard the production of the specific zymogen not as the formation of a new body, but as resulting from an alteration in the atomic arrangement within the protein molecule and a consequent change in its chemism.

4. Some proteins in developing the specific zymogen, produce profound and lasting changes in molecular structure, while the alterations induced by others are slighter and of temporary duration, the molecular structure soon returning to its original condition.

² Jour. Infect Dis., 1907, iv, 476.

5. Bacteria and protozoa are living, labile proteins; while egg-white, casein, serum albumin, etc., are stable proteins. The proteins of the one group are in an active, and those of the other in a resting state, but both are essentially proteins, made up of an acid or poisonous chemical nucleus and a basic or non-poisonous group. The former in its effects upon animals is the same whether derived from the living or the dead protein, and the latter in the one instance induces specific immunity and in the other specific susceptibility; but the immunity and susceptibility each consists in developing in the animal body the capability of splitting up a specific protein. If the living protein be split up before it has time to multiply sufficiently to furnish a fatal quantity of the poison the animal lives and we say that it has been immunized. If the stable protein be introduced into the animal it leads to the development of a specific proteolytic ferment, and if enough of it to supply a fatal dose be reinjected after this function has been developed, the animal dies. The first or sensitizing dose of egg-white injected into an animal is digested just as surely as is the second, but the process goes on so slowly that we see no effect, but in fact the first dose has affected the animal profoundly, so profoundly that the change wrought in certain cells of the animal body persist for months, possibly for years, and may be transmitted from the mother to her offspring. We do not say that the animal is sensitized unless some immediate and striking effect follows our treatment, but this is wrong. An immediate effect, especially a fatal issue, on reinjection, depends upon the rapidity with which the protein is split up and its poisonous constituent set free. The sensitizing injection leads to the development of a specific enzyme and the protein of this injection is so slowly digested that the poison set free at any one time is not sufficient to produce any recognizable effect. If time enough be allowed between the sensitizing and the reinjection for the accumulation of a large amount of the specific enzyme, then the protein is split up promptly and anaphylactic shock and death result. These views concerning protein sensitization first offered in 1907, have been on the whole, confirmed by later investigators.

The fact that an animal is sensitized before the time when a reinjection is followed by anaphylactic shock has been conclusively demonstrated by inducing passive anaphylaxis with serum taken from animals in the so-called preanaphylactic state. Likewise it has been shown that serum taken from animals in the so-called antianaphylactic state passively sensitizes fresh animals.

The Prevention of Anaphylactic Shock. From a practical standpoint anaphylactic shock is the least important of the phenomena of sensitization. It is always an artificially induced condition, and the only importance it brings to the practitioner is that he should know how to prevent it in serum therapy. Although the

procedure necessary to protect the patient against anaphylactic shock was first pointed out by Vaughan, Jr., the best work along this line has been done by Besredka. The last-mentioned investigator has shown that the intraperitoneal injection of from $\frac{1}{50}$ to $\frac{1}{100}$ c.c. of the serum in sensitized guinea-pigs renders them so positively refractory that five hours later intracerebral injections are wholly without effect. Besredka has made quite a thorough study of the means by which anaphylactic shock in serum therapy may be averted and he states his conclusions as follows:

1. Preparatory heating of therapeutic sera to 56° tends to suppress the phenomena of sensitization without wholly averting them. Besredka states that all therapeutic sera prepared at the Pasteur Institute are subjected to this temperature, and that instances of anaphylactic shock are less frequent, and, when seen, less severe in France than in countries in which this preliminary heating is not practised.

2. Aleoholic and ether narcosis give a complete, but transitory, immunity to anaphylactic shock. (This is not practical.)

3. Preventive injections of serum heated to 80° produce a certain and lasting immunity, but it develops slowly and is accompanied by slight reaction. (It will be understood that only that portion of the serum used to prevent anaphylactic shock is heated to this temperature, which would render antitoxin inert.)

4. The best method of averting anaphylactic shock is either by rectal injection of the unheated serum, or better still, by the subcutaneous injection of a very small dose.

The recommendation of Vaughan, Jr., is that in all cases in which anaphylactic shock may be feared a preliminary injection of from 0.1 to 0.2 c.c. should be made, and after an interval of two hours, provided no untoward symptoms have appeared, the full dose may be given. The suggestion is made by Rosenau and Anderson that all individuals who have shown any tendency to asthma, together with those who have received previous injections of the serum, with an interval of twelve days or longer, should be included among those in whom anaphylactic shock may be feared. It is not held that even with these precautions all the symptoms of serum disease will in all cases be averted, but serious anaphylactic shock is not likely to occur.

Serum Disease. The studies of v. Pirquet and Shiek³ on diseased conditions induced by therapeutic sera have proved of great value in explaining the phenomena of protein sensitization. In a certain percentage of individuals who receive injections of horse serum for the first time certain well-defined symptoms develop, usually from six to twelve days after the injection. The symptoms consist of fever, more or less general edema and rash, generally urticarial,

³ Die Serumkrankheit, 1905.

though sometimes erythematous. The rash is usually accompanied by intense itching and it may cover not only the entire surface of the body but extend to the visible mucous membrane of the mouth and throat, about the anus, and into the rectum. The lymph glands may be enlarged, and pain in the joints is often severe. The percentage of persons thus affected by the first dose of horse serum increases with the quantity of serum employed. The explanation offered by v. Pirquet is that some of the unchanged serum remains in the body until sensitization is sufficiently developed to "bring the effects of the toxic body up to the level of clinical observation." This demonstrates that a reinjection is not necessary in order to develop the state of protein sensitization. The evolution of the specific enzyme begins soon after the introduction of the foreign protein and gradually proceeds, and the liberation of the protein poison increases *pari passu*. It is not until the effects of the liberated poison approach the "level of clinical observation" that we recognize them, but this is not at the beginning of the process. Sensitization of the body cell probably begins as soon as the foreign protein comes in contact with it. The foreign protein so impresses the body cell that the latter undergoes such changes in its intramolecular structure that it elaborates a new and specific enzyme. The fact that soluble proteins sensitize so much more promptly and efficiently than suspensions renders it probable that cellular penetration is essential to the most thorough effect. The additional fact that relatively dilute solutions sensitize more promptly and more efficiently than more concentrated ones suggest that degree of molecular concentration has some influence upon the processes of sensitization.

Von Pirquet and Shick observed two kinds of reaction in those who received reinjections after intervals of twelve days or longer. In some the reaction is of the same character as that described above, but it appears two or three days earlier. It is supposed that those in whom this form, designated as "accelerated reaction," occurs, have partially passed beyond the condition of sensitization, but easily resume it on receiving the reinjection. There seems to be no danger to life in either the "delayed" or "accelerated reaction." The one accompanied by marked danger to life is the "immediate." In this the effects manifest themselves within a few hours, often within a few minutes, after the reinjection. These individuals are in a fully sensitized condition, and it is in these that anaphylactic shock should be feared.

There are instances in which the first injection of horse serum has induced alarming, and rarely fatal, anaphylactic shock. These have been reported with sufficient frequency to cause more or less anxiety in the employment of therapeutic sera; besides, it raises the very important question as to why a small percentage of persons should be, apparently naturally, susceptible to an agent

to which the great majority are immune. Cases of "horse asthma," in which more or less violent symptoms, such as sneezing, inflammation of the conjunctiva and the mucous membrane of the upper air passages result from riding behind horses are well known. The flying hairs from horses carrying minute quantities of protein are inhaled and may cause local sensitization, and it may be that this accounts for the instances of anaphylactic shock observed after first injections of horse serum. The recent brilliant work of Rosenau in which he has shown that the expired air contains a protein sensitizer seems to explain sensitization to horse serum.

Vaccination. The valuable research of von Pirquet⁴ on vaccinia has done much to elucidate the problems of sensitization. By daily vaccinations this investigator has shown that the process is accelerated until finally it passes through every phase in a few hours.

This explains not only the development of vaccinia and the way in which it protects against smallpox, but also vaccination in other infectious diseases. The avirulent organism of vaccinia still has the protein constitution of the virulent one of smallpox. It has been modified in function but not seriously altered in essence by its passage through the cow. The proteins constituting its molecules have not been changed, or if at all, so slightly altered that one form still sensitizes to the other. The modified virus sensitizes the body cells and by this we mean that it causes the cell to elaborate a specific enzyme that digests and destroys the virus. The body cells retain this new function and when the smallpox virus finds its way into the body it is digested and destroyed before it has time to multiply sufficiently to cause disease. This is the basis of all bacterial and protozoal vaccination. In securing his vaccine for chicken cholera Pasteur modified the organism by successive growths on artificial culture media. That for anthrax he obtained by growth at relatively high temperature, and that for rabies by drying the cord. The vaccine for typhoid fever is obtained by the use of cultures killed by heat. All these processes in the special instances modify the proteins of the organisms so slightly that they still sensitize to themselves. This is protein sensitization and gives protein immunity. It is wholly different from toxin action and toxin immunity and we should not confuse the two by discussing one in terms of the other. In protein immunity there is no antigen and no antibody, and we will proceed more understandingly if we stop employing these terms in discussing protein sensitization. The toxins are either ferments or closely related bodies, and the substance that digests the protein on reinjection or in the sensitized state of the animal is a ferment, and it is proper to speak of it as consisting of amboceptor and complement, but further

⁴ Klinische Studien über Vakzination u. Vakzinale Allergie, 1907.

than this the nomenclature introduced by the genius of Ehrlich to explain toxin action and reaction has no place in the literature of sensitization.

If what has been stated be true, protein sensitization is a most important factor in acquired immunity and it will be well to discuss methods of using so powerful an agent in combating disease. It should always be held in mind that every protein contains a powerful poison, and that no unbroken protein can be injected into the body without carrying with it this poison, and moreover, the parenteral digestion of a protein means that its poisonous group will be set free or activated in the body. The liberation of this poison occurs not in the alimentary canal, the walls of which may protect the body or from which it may be rejected by vomiting or purging, or by both, but in the blood and tissue, and there is no escaping its effects. It is a poison, not a toxin, and there is up to the present time no known antidote for it. The indiscriminate employment of protein injections now being made should be most positively condemned.

Work done in my laboratory indicates that with some proteins at least the sensitizing and poisonous groups may be separated, and that when this is done the former sensitizes quite as efficiently and sometimes much better than the unbroken protein containing its poisonous group. In animals the non-poisonous part of the typhoid protein gives immunity to the living bacillus to a much greater degree and more promptly than the unbroken bacillus, either alive or dead. It is freely soluble and the more soluble protein sensitizers are the more promptly and efficiently do they act. However, this needs more thorough study and tests should be made on man.

That the tuberculous animal behaves differently from the non-tuberculous on receiving injections of the tuberculin protein, whether it be in the form of the living bacillus, in dead cells, or in solution, has been abundantly demonstrated. Before Koch gave us tuberculin, Aloing and Courmont had come to the conclusion that the tubercle bacillus produces soluble substances which reduce the natural resistance of the body and render it more susceptible to reinfection. This corresponds closely with the first impression made by observation of the phenomena of anaphylaxis; the impression that led Richet to select this term. In 1891, Koch described a perfect example of protein sensitization as we understand it today. He stated that when a healthy guinea-pig is inoculated with the living tubercle bacillus there is no change at the site of inoculation until from ten to fourteen days later, when a hard lump forms, finally opens and ulcerates, and continues until the animal dies. On the other hand, when a tuberculous guinea-pig is inoculated with the living bacillus, on the second or third day a lump forms, soon becomes necrotic, falls out, ulcerates for

a time, and finally, heals without any infection of the neighboring lymph glands. In 1897, Trudeau observed that when healthy rabbits receive injections of virulent cultures in the eye, there is little to be seen for about fourteen days, when with increasing vascularity tubercles form in the iris after which inflammation extends and the eye is practically destroyed within from six to eight weeks. Like treatment of tuberculous rabbits develops an iritis within from two to five days, but at the end of the second or third week at a time when the controls begin to develop destructive changes the inflammation begins to subside. Later studies have confirmed and amplified these, and it has been found that death may be induced within twenty-four hours by injecting a large amount of a living culture into a tuberculous animal.

The same difference between healthy and tuberculous animals has been observed in their response to injections of dead cultures of the tubercle bacillus. The first observation along this line, so far as I know, was made by Strauss and Gamalcia, who found that when large numbers of dead tubercle bacilli are injected into tuberculous animals death results, while similar amounts are without immediate effect upon healthy animals.

When we come to tuberculin, every phase of its action or its failure to act is explainable on the ground that the tuberculous animal is a sensitized one. Koch found that 0.5 gram of his preparation killed tuberculous guinea-pigs, and induced no symptoms in healthy ones. A fraction of 1 milligram may cause marked symptoms in a tuberculous man, while many times this amount is borne easily by a healthy man. The inflammatory reaction about local tubercular lesions caused by injections of tuberculin is explained by the fact of the high degree of sensitization in their localities, and the cleavage of the bacilli. The ophthalmic, cutaneous, subcutaneous, and intravenous tests with tuberculin are all typical sensitization reactions. Even in the failure to respond to tuberculin seen in advanced tuberculosis we have the condition known as antianaphylaxis, which simply means that the anaphylactic ferment is exhausted by the large amount of material supplied by the bacilli in the body.

There is another line of evidence that in tuberculosis there is a condition of specific protein sensitization. This is to be found in the fact that this disease is much more deadly in lands and among people who have recently come under its influence than it is where it has prevailed for many generations. In other words, the widespread and long-continued existence of the disease, slowly, and at the cost of much sickness, and many deaths, brings a certain degree of immunity. The readiness with which the North American Indian has succumbed to this disease is a striking illustration, and Calmette has recently collected additional evidence on this point. He states that tuberculosis is being widely disseminated

among peoples who have until recently been free from it. The world-wide wanderings of the white man are carrying the disease to every people, from the Laplander and Esquimaux of the Arctics to the negroes and Malays of the tropics. Iceland, the Faro Islands, and the steppes of Russia are being infected, and in these new regions tuberculosis exists in its most speedily fatal forms. The same author points out that recently discovered methods for the recognition of this disease, even in latent states, shows that among Europeans not more than 7 or 8 per cent. reach more than twenty years of age without receiving the infection. Those who survive the first infection become more or less immune, and after that develop when they do acquire the disease the more chronic forms.

Römer⁵ concludes that the less widely tuberculosis is distributed among a people the greater is the case mortality, and the wider the distribution the smaller is the case mortality.

Still another fact of importance is that the most speedily fatal forms of tuberculosis, such as the miliary and meningeal, are more frequent among children than among adults.

There is another matter of much importance in this connection which we must discuss. We have found the tubercle bacillus highly resistant to lytic agents, and it appears that its long experience as a parasite has led it to protect itself with deposits of wax and fat, but proteolytic enzymes digest the most firm proteins. Friedberger has found that at least some strains of this bacillus are digested by the serum of healthy guinea-pigs, and the researches of Markl, Bail, and Kraus and his students have shown that tubercle bacilli placed in the peritoneal cavity of tuberculous animals respond to Pfeiffer's reaction. Some strains are dissolved in the peritoneum of healthy guinea-pigs, but dissolution occurs more promptly and more completely in the peritoneum of a tuberculous animal. The healthy animal may have to depend upon its phagocytes to combat the invading bacillus, but the tuberculous animal supplies a specific proteolytic enzyme, and to this the fresh invader succumbs.

Nature is slowly immunizing the white man to tuberculosis, and the question arises whether or not the process employed by nature can be aided in any way. There is before the medical profession at this time no greater question than this: Is it possible to aid in eradicating tuberculosis by vaccination? As Römer says, the problem of securing immunity to tuberculosis with a non-infective virus is of great practical importance and recent work brings the possibility of doing this more and more to the front. What we need is a vaccine. Various methods of modifying the tubercle bacillus so that it could be used as a vaccine have been tried. The bovo vaccine of von Behring was tried, but the increased resistance given by it was found to be of short duration.

⁵ Beiträge z. klinik. d. Tuberk., 1912, xxii, 301.

Attempts to reduce its virulence by age, heat, chemicals, and by submitting it to ultraviolet and other rays and emanations have been made. What we need is a tubercle protein sensitizer. It should be soluble, and it should be free from the poisonous group in the protein molecule. In my opinion the nearest approach to this desired substance is the non-poisonous portion of the tubercle protein. So far we have not been able to secure a uniform product. Some preparations seem to fill every requirement. They sensitize animals to the unbroken bacillus, dead or alive, and in surface tuberculous lesions they cause inflammation about the tuberculous area, and we have seen the tuberculous tissue slough off and complete recovery result; but other preparations made from the same cellular substance by the same method seem inert. We have had similar difficulties with the sensitizing groups from other proteins. Some preparations from egg-white sensitize to unbroken egg-white, while others seem wholly without effect, and still all are prepared from the same material and in the same way. Evidently the sensitizing group in the protein molecule is a highly labile body and susceptible to influences which so far we have not been able to recognize. We have no difficulty in obtaining the poisonous group uniformly, but it is otherwise with the sensitizing body. Further work along this line is needed, and if an efficient and uniformly reliable sensitizer for the tubercular protein, free from the poisonous group, can be secured, all children should be vaccinated for tuberculosis; then with protection against natural infection the restriction of tuberculosis will be as completely under man's control as is that of smallpox. It should be clearly understood that the protection afforded by vaccination is relative and not absolute.

The studies inaugurated by Wright have demonstrated that vaccination is of service not only in prevention, but also in cure. Bacteria and protozoa are particulate, and in many diseases they are confined to limited localities. As we have seen, sensitization may also be local. No body cell is sensitized against a foreign protein until the latter comes in contact with the former and penetration of the body cell is probably essential to the most efficient sensitization. The microorganisms of acne are located in the cutaneous tissue and being particulate and not in solution, the area sensitized by them is small, if there be any sensitization at all. By vaccine therapy the area of sensitization is greatly extended and the amount of lytic agent formed and made available is greatly increased. This being in solution and diffusible, digests and destroys the bacteria located in the skin. The same is true of the treatment of localized tuberculosis, or of any other localized infectious disease. In vaccine therapy, as in vaccination, the great need is for soluble sensitizers free from poisonous content. When these are secured, and not until then, we may develop a vaccine therapy along scientific lines, and expect to secure important results with it.

Fever. It is interesting and instructive to read the older literature on fever in the light of the knowledge which has been gained in the study of sensitization. It has long been known that the parenteral introduction of proteins in small amounts and especially repeated introduction, leads to fever. The older literature on this subject as well as an account of his own work was given in 1883 by Roques.⁶ In 1888, Gamaleia⁷ showed quite clearly that fever accompanies and results from the parenteral digestion of bacterial proteins, and a year later Charrin and Ruffer⁸ confirmed this work and extended it to non-bacterial proteins. In 1890, Buchner⁹ produced the characteristic phenomena of inflammation—color, rubor, tumor; and dolor—by the subcutaneous injection of diverse bacterial protcins. In 1895, Krehl and Matthes¹⁰ induced fever by the parenteral introduction of albumoses and peptons, but they did not obtain constant results, which we now know are secured only by regulation of the size and frequency of the dosage. In 1909, Vaughan, Wheeler, and Gidley¹¹ demonstrated that any desired form of fever—acute fatal, continued, intermittent, or remittent—can be induced in animals by regulating the size and frequency of the doses of foreign protein administered parenterally, and in 1911, Vaughan, Cumming, and Wright¹² extended the details of this work. These investigators established the following points:

1. Large doses of unbroken protein administered intra-abdominally, subcutaneously or intravenously, have no effect upon the temperature; at least, do not cause fever.

2. Small doses, especially when repeated, cause fever, the forms of which may be varied at will by changing the size and the interval of dosage.

3. The effect of protein injections on the temperature is more prompt and marked in sensitized than in fresh animals.

4. The intravenous injection of laked blood corpuscles from either man or the rabbit causes in the latter even in very small quantity, either in single or repeated doses, prompt and marked elevation of temperature.

5. Laked corpuscles after removal of the stroma by filtration have a like effect.

6. Protein fever can be continued for weeks by repeated injections, giving a curve which cannot be distinguished from that of typhoid fever.

7. Protein fever is accompanied by increased nitrogen elimination and gradual wasting.

8. Protein fever covers practically all cases of clinical fever.

⁶ Substances Thermogenes, Paris, 1883.

⁷ Ann. de l'Institut Pasteur, xii, 229.

⁸ Comp. Rend. Soc. de Biol., 1889, 63.

⁹ Berl. klin. Woch., 1890, 216.

¹⁰ Arch. f. exp. Path. u. Pharm., 1895, xxxv, 232.

¹¹ Jour. Amer. Med. Assoc., August 21, 1909.

¹² Zeitsch. f. inner. Medizin, ix, 458; Trans. Assoc. Amer. Physicians, 1911.

9. Animals killed by experimentally induced fever may die at the height of the fever, but as a rule, the temperature rapidly falls before death.

10. Fever induced by repeated injections of bacterial proteins and ending in recovery is followed by immunity.

11. The serum of animals in which protein fever has been induced digests the homologous protein *in vitro*.

12. Fever results from the parenteral digestion of proteins.

13. There are two kinds of parenteral proteolytic enzymes, one specific and the other non-specific.

14. The production of the non-specific ferment is easily and quickly stimulated.

15. The development of the specific ferment requires a longer time.

16. Sensitization and immunity are different manifestations of the same process.

17. Foreign proteins, living or dead, formed or in solution, when introduced into the blood soon diffuse through the tissues and sensitize the cells. Different proteins have predilection places in which they are deposited and where they are, in large part at least, digested, thus giving rise to the characteristic symptoms and lesions of the different diseases.

18. The subnormal temperature which may occur in the course of a fever or at its termination is due to the rapid liberation of the protein poison, which in small doses causes an elevation, and in larger doses a depression of temperature.

19. Fever *per se* must be regarded as a beneficent phenomenon, inasmuch as it results from a process inaugurated by the body cells for the purpose of ridding the body of foreign substances.

20. The evident sources of excessive heat production in fever are the following: (a) That arising from the unusual activity of the cells supplying the enzyme; (b) that arising from the cleavage of the foreign protein; (c) that arising from the destructive reaction between the split products, from the foreign protein and the proteins of the body.

In 1910, Friedberger¹³ studied the effects of graduated doses of foreign proteins on the temperature of both normal and sensitized animals. With lambs' serum intravenously administered to normal guinea-pigs he obtained the following results:

5.0	c.c. equals fatal dose.
0.5	c.c. equals limit for fall in temperature.
0.01	c.c. equals upper constant.
0.005	c.c. equals fever plane.
0.001	c.c. equals lower constant.

¹³ Berl. klin. Woch., 1910, No. 42.

In sensitized guinea-pigs the above figures were changed to the following:

0.005	c.c. equals fatal dose.
0.0005	c.c. equals limit for fall.
0.00001	c.c. equals upper constant.
0.000005	c.c. equals limit for fever.
0.000001	c.c. equals lower constant.

In 1911, Schittenhelm, Weichardt, and Hartmann¹⁴ experimented upon the effect of the parenteral administration of diverse proteins on animal temperature and came to the following conclusion, which in my opinion, is well stated: "In severe experimental anaphylaxis there is a fall in temperature; in the lighter manifestations there is fever." We regard this as a confirmation of our conclusion reached some years earlier. "Small, especially repeated, doses of the protein poison cause fever, while large doses depress the temperature."

Some years ago Friedmann and Isaak¹⁵ showed that after the parenteral introduction of foreign proteins the increase in nitrogen elimination is greater than can be accounted for by the protein injected. This has been confirmed by the work of Schittenhelm and Weichardt¹⁶ and as has been stated, we found the same in protein fever. Our explanation for the marked increase in nitrogen elimination has been given.

In intermittent and remittent fevers and in relapses in all infectious diseases the phenomena of protein sensitization are fully demonstrated. In the different forms of malaria, chill and fever correspond to the discharge of foreign protein into the blood, just as promptly as anaphylactic symptoms follow the injection of the homologous protein in a sensitized animal. The moment the blood cells rupture and the protozoal protein is disseminated the sensitized cells discharge the lytic ferment by which the foreign protein is disrupted and destroyed, but in this process the poison is liberated.

Local sensitization is frequently established in the mucous membrane of the air passages and of the alimentary canal, also in the skin for two reasons. In the first place, foreign proteins are frequently brought into direct contact with these tissues, and in the second place, foreign proteins introduced into the blood are frequently deposited in the skin and in the walls of the alimentary canal. These local sensitizations characterize many of the infectious diseases. The work of Dunbar and Weichardt on hay fever is a nice illustration. These investigators injected each other subcutaneously with minute quantities of pollen suspension. Immediately Dunbar, being a hay-fever subject, became dizzy and within a few minutes began to sneeze, then a whooping-like

¹⁴ *Zeitsch. f. exp. Path. u. Ther.*, 1911.

¹⁵ *Ibid.*, 1905, 1906, and 1908.

¹⁶ *Zentral. f. d. ges. Physiol. u. Pathol. d. Stoffwechsel*, 1910.

cough began. The eyes were congested, and an abundant secretion flowed from the nose. The face became swollen and cyanotic, and soon the body was covered with an urticarial rash. After twenty-four hours these symptoms subsided. Weichardt, not being a hay-fever subject, was not affected. That this and kindred affections are not benefited by antisera was abundantly and positively demonstrated by the failure of the so-called hay-fever serum, which was found in no instance to be of special value, and in some it greatly intensified the symptoms.

Our common colds, are instances of local sensitization. Sehittenhelm and Weichardt tell of a man who was so deeply sensitized by the inhalation of Witte's pepton that he could tell on entering the laboratory whether the pepton flask was open or closed, and some moist pepton painted on the skin caused the area covered to become red. The high degree of susceptibility to odors from the horse shown by some people has already been referred to. It seems in some instances that this susceptibility is transmitted from mother to child.

A volume might be filled with citations of cases of food and medicine idiosyncracies. That these are, in large part at least, instances of protein sensitization has been demonstrated by rendering animals susceptible to the same food or medicine by injecting them with the serum of the susceptible individual. In other words, passive anaphylaxis has been established in the animal. In this way Bruck has sensitized animals to iodoform and antipyrin with the sera of persons especially susceptible to these agents.

We are compelled to change our ideas concerning the causation of the lesions of the infectious diseases. Formerly we believed the structural changes to be due wholly to the living, growing, feeding microorganisms. For instance, we were sure that the intestinal ulcerations of typhoid fever are caused by the living bacilli. Now we know that these lesions follow the intravenous injection of dead proteins. As has been stated, each foreign protein has its predilection tissue in which it is largely deposited, whose cells it especially sensitizes, and where it is disrupted. This explains the characteristic lesions and symptoms of the different infectious diseases. As I stated in the Shattuck Lecture of 1906: "Bacterial inflammation is essentially a chemical process, or is due to the disruption of cell molecules through the chemical affinity between certain groups in the bacterial cell and certain groups in the cell of the animal. So long as the bacterial cells are alive the chemism that holds the living molecule together tends to resist this process of disintegration. . . . The pathogenic bacterium assimilates the nutritious constituents of the fluids of the animal body, builds them into its own tissue, converts them into substances foreign to the host and, finally, when the bacterial cell goes to pieces either from spontaneous dissolution, or through the aggressive action of

some animal cell, these reconstructed chemical groups are set free and poison the animal, inducing lesions in various tissues, and, in many instances, so interrupting the vital functions as to cause death." It is in harmony with these statements that Friedberger has been able to induce aseptic pneumonia by spraying horse serum into the lungs of guinea-pigs sensitized with the same, and Schittenhelm and Weichardt have established "enteritis anaphylactica" by the reinjection of egg-white into sensitized dogs. It is more than probable that cholera infantum and the kindred summer diarrheas result from the absorption of undigested milk and consequent sensitization. The designation "protein diseases" might be used to cover the majority of bacterial and protozoal diseases, and many of these hitherto regarded as auto-genous.

CONCLUSION. In conclusion, I wish to state that all the problems of protein sensitization have not been solved. It seems to be a physiological law that the specific ferments elaborated by living cells are determined by the proteins brought into contact with them, but as yet we know but little concerning these bodies which we call ferments. That they are labile chemical bodies resulting from intramolecular rearrangement in the protein molecules of the cell seems a plausible theory, but at present it is only a theory. We know but little of the action of these so-called ferments upon their homologous proteins. Our knowledge of the chemistry of protein sensitizers is exceedingly limited, and as I have pointed out, it is highly desirable that work in this direction should be prosecuted with vigor, because we need sensitizers free from the poisonous group. Furthermore, there is the question, why small doses of protein induce fever while large doses have no such effect. At present we have no satisfactory answer to this question. If it could be conclusively demonstrated that the toxins are ferments, the subject of the etiology of disease would be greatly simplified. I have elsewhere¹⁷ given my reasons for holding that the toxins are ferments, and in closing this paper I wish to formulate what I believe to be two biological laws:

1. When the body cells find themselves in contact with, or permeated by, foreign proteins they tend to elaborate specific ferments which digest and destroy the foreign proteins.
2. When body cells are attacked by destructive ferments they tend to elaborate antiferments the function of which is to neutralize the ferments and thus protect the cells.

¹⁷ Trans. Assoc. Amer. Physicians, 1911.

CHRONIC PURPURA, AND ITS TREATMENT WITH ANIMAL SERUM.

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THE object of the writers in presenting this article to the profession is to call attention to chronic purpura, place on record the histories of two cases of the disease, and report the results of the treatment of this comparatively rare and protean disease with animal serum.

Discouraged by his repeated failure to influence the disease by the ordinary forms of treatment of purpura as originally summarized by Davis King, Jr., in his Fisk Prize Essay (1836), and modified during recent years, the writer was ready to welcome the facts to which Weil¹ called attention in connection with the use of animal serum in the treatment of purpura, and was pleased to coöperate with his coworker in this article (Meader) in the application of the remedy by the latter to the treatment of the cases included in this article, and to other forms of purpura and hemorrhagic disease less chronic than those herein reported.

Weil's work brought out these facts: that the blood serum of horses, rabbits, and beef creatures, as well as human serum, had the power of controlling hemorrhagic processes by increasing the coagulability of the blood; that beef serum was too toxic for ordinary use; that the serum used should be less than two weeks old; that a dose of 15 c.c. intravenously or of 30 c.c. subcutaneously would obtain results in most cases; that the use of serum locally at the point of hemorrhage favored clotting; that the increased coagulability of the blood persisted for a period of from fifteen days to several weeks after injection.

CASE I.—Mrs. H. W. J.; first seen December 24, 1905; aged forty-five years; family history excellent, without taint; great resistance; no specific history. Patient is a woman of splendid education and refinement, who has always lived a temperate and exemplary life, devoting much of her time to study and painting. She has no living children; nine years ago had a miscarriage. Soon after this it was found that she had a uterine fibroid and ovarian cysts, for which a complete hysterectomy was successfully performed. Otherwise she had always been well. Much of her time was spent in the open air, during the summer months on the coast of Maine. When I saw the patient in 1905 she had a severe left

¹ P. Emile, *L'Hemophilie*, etc., *Press Médical*, October 18, 1905.

brachial neuritis, was anemic, reduced in flesh, and excessively nervous, but without discoverable physical signs of cardiac or other disease. The neuritis yielded to tonic treatment and high frequency. Within one year after the cure of the brachial neuritis she had an acute suppurative disease of the antrum of Highmore, which was relieved by the usual surgical treatment, but required continuous drainage for three years. The drainage tube was in the antrum when the patient consulted me January 17, 1908. I found her suffering greatly from pains, rheumatic in character, in both legs; joints painful, but no swellings noticeable. She had large varicosities, and considerable infiltration of the skin in spots over the shins, the characteristic and usual accompaniment of long-continued venous stasis. Under rest, tonic treatment, and well-fitting stocking support there was decided improvement of symptoms referable to the extremities until April 11, 1908, when I found her with fully developed purpura rheumatica; both legs were involved; purpuric lesions numerous, more on the left than on the right leg; some of the spots were as large as a silver dollar. Some of the purpuric macules were ecchymotic, others bright red. There were macules on the arms, on the abdomen, and a few on the face. The patient volunteered the information that possibly her condition might have been aggravated by the inhalation of sewer gas. Thorough physical examination failed to show heart murmurs, there was more or less malaise; pulse was small but regular, 88; arteries normal. Systolic blood pressure 110, diastolic 75; pulse pressure, 35. The examination of the urine at this time gave negative results; no abnormalities in the proportion of its solid constituents were found. Blood examination showed a slight polycythemia: reds, 6,200,000; hemoglobin, 100; whites, 12,000. Blood platelets unfortunately were not counted at this time. Stained smear showed but little variation in size; a few poikilocytes. A few leukocytes resembling myelocytes were seen. Polymorphonuclears, 84 per cent.; lymphocytes, 14 per cent.; eosinophiles, 2 per cent. Time of coagulation of blood was normal. Blood cultures have always been negative. In a few days (April 21) a purpuric spot, which was about the size of a nickel on the plantar surface of the right foot, became exquisitely tender and so painful that the patient was kept awake by it; there was a great deal of pain in the right foot, which was swollen, and in the course of three days the tender spot on the sole showed positive evidences of localized gangrene, corresponding in size with the original area of purpura. In due time the necrobiotic patch showed a distinct line of demarcation, and by April 29 the superficial slough had lifted itself; the odor was characteristic of dead tissue. On that day the following note was made: "Patient has new purpuric spots on left ankle. Has swelling of the small joints of both hands, but is without fever."

These rheumatic symptoms continued during several days; finally the hands became purpuric and the pains were relieved. Aspirin seemed to relieve the pains. Gave aromatic sulphuric acid with quinine, nutritious diet, fruit acids, abundant salt, without in any way controlling the purpuric symptoms.

May 8. "Some improvement; a few purpuric spots are fading. On the sole of the right foot there is a new patch of superficial death of the purpuric macule, larger than the first, almost the size of a fifty-cent piece. There are a few erythematous spots over the knuckles of both hands. No fever. Pulse, 78."

May 11. "No new symptoms. The spots on the sole of the right foot emits the usual odor of infarct and final superficial gangrene. There are petechiæ here and there over the entire body, face and arms included."

May 26. "New purpuric spots and joint symptoms follow wherever the patient scratches or strikes herself, or where undue pressure is exerted. In some of these gangrene follows. Discontinued the acid and substituted calcium lactate and phosphomuriate of iron and quinine with the same diet. Never yet have I found the patient with fever."

June 1. "No new spots today unless she pricks herself, then the tendency to superficial breakdown continues."

June 2. "New crop of purpura over legs, ankles dotted, and on the face. 'Hemorrhagic lines' are noted on the abdomen a few following skin irritation or scratching. There are (June 10) a number of erythematous patches around the larger joints of the body."

June 13. Patient was placed in charge of Dr. John Van Duyn, who continued to treat her until my return from abroad on September 19, 1908, when the following note was made: "There has been but slight improvement; the hollows of both feet are healed; the purpura is general; has a troublesome erythema and intertrigo, with eczema in axillæ, groins, and other folds of the body. Ankles are swollen; the purpuric spots on the lower extremities particularly near the ankle are large and of a deep purple color." During the following six months the skin irritation became general and made the patient very wretched. There was scarcely a time when with more or less eczema and intertrigo there was an absence of fully developed Werlhof symptoms, including tenderness of the gums, and some bleeding from these on slight cause. There was no hemorrhage from the internal organs. There was, however, an occasional nose-bleed. This may have been due to the crusting and ulceration of the mucosa. On one occasion a purpuric spot on the right side of the nose sloughed. It would be useless to present the full history of this case during the almost three years following, as it would be a repetition of all that has been given. It can be easily understood from the following short abstract:

Patient continued to present some of the lesions originally present almost continuously; there never was a time when she did not show purpuric spots on both extremities; at times there was an addition during several days of purpura rheumatica. The intertrigo was finally controlled and has never recurred. There have been varying periods of spongy gums, with some bleeding. Until we commenced the use of the animal serum, preceded by the vaccine to be mentioned later, the patches of local death, particularly on the plantar surfaces of both feet and around the finger nails, continued exceedingly annoying, and recurred at short intervals. During the past four years the patient has been treated for purpura; the urine has continued normal, save at times when there has been slight bladder irritation, then a faint trace of albumin has been found, and on one occasion there was albuminuria for several days after the injection of the serum. There have been times when either because of the visceral symptoms due to the disease, oftener to the medication, there have been painful gastro-intestinal disturbances. It was found during the second year of treatment that there was but one drug combination which influenced the symptoms in any way, and this proved to be the elixir of the four chlorides, which in turn, when taken during a long period, caused griping and diarrhea. The effect was so beneficial in the general improvement and in the partial control of hemorrhagic symptoms that the patient of her own volition continued the remedy until forced to discontinue for short periods, when she again returned to its use. The bichloride of mercury alone or arsenic alone had no influence on the course of the disease. The iodides invariably aggravated the symptoms. It can be easily understood that during these years many remedies were tried and many suggestions followed. Urotropin among these was without effect.

If we were to summarize this case from early 1908 until January 13, 1911, when we found a small pustule on the right leg of this patient from which a vaccine was made, we would present the characteristic picture of chronic purpura without intermission, never a time when the patient was free from some of the lesions of the disease, with repeated circumscribed gangrenous patches following purpuric macules. At no time were the symptoms of the disease limited to one type of purpura; the lesions were indiscriminately distributed, a mixture of all types, corresponding, however, more closely to the continuous type of chronic purpura described by Bensaud and Rivet.²

On January 13, 1911, the authors saw the patient together for the purpose of considering the advisability of giving a normal animal serum or a vaccine which might be elaborated. A small purpuric spot was found covered by a pustule about the size of

² *Archiv. Générale de Médecine*, December 1, 1905

a split pea; from this a pure culture of *Staphylococcus aureus* was made, which gave a vaccine. The patient received three injections respectively: 50,000,000, 100,000,000, 250,000,000 of the vaccine January 16, 20, and 24. By January 20 the general condition was not disturbed by the vaccine; new purpuric spots continued to appear, but the necrobiosis was favorably influenced by the vaccine.

January 27. 17 c.c. horse serum were injected into the left abdominal wall. This was followed by severe pain, which subsided in several hours.

January 31. The surface looks less blotchy; until today there have been no fresh petechiæ; a few spots were noticed on the fingers about the knuckles; these were erythematous, not hemorrhagic. Urine was slightly albuminous; no casts.

February 6. Today an injection of 10 c.c. horse serum was given, promptly followed by general erythema, which covered the entire body, and tender and painful joints, such as are met after the injection of antidiphtheritic serum.

February 7. Joint pains severe; general erythema multiforme persists. Temperature, 98°; pulse, 78; respirations, 19. There is but one fresh petechia on the patient, and that on the left knee.

From February 6 to 16 inclusive the serum sickness persisted, and included besides the erythema, severe headache, which finally yielded to quinine and sodium salicylate.

From February 16 until March 20 there was decided improvement in all the subjective and objective symptoms. The patient was able to be about, there were no fresh petechiæ, the ecchymotic spots of the old lesions were fading, the joints were normal and in every way the condition was better than it had been in almost three years.

During March and April and until May 15 the patient made material progress, was exhilarated, seemed to be "living in a new world," was happy, and encouraged. She required no medical attention, because the symptoms were held in abeyance, and there were only occasional small cutaneous lesions.

May 15. If patient tires after exertion she notices a few fresh "spots." She walks well. Today there are a number of hemorrhagic macules on both lower extremities over the left knee. In spite of the severe serum sickness which she had after the last injection its effect appears to her so beneficial that she literally "begged for it" today. *Since the use of the vaccine and the serum the antrum has closed.* Barring a recent slight hemorrhagic gingivitis there are no symptoms referable to the buccal or nasopharyngeal mucosæ. There has been no tissue loss about the fingers (hemorrhagic panaritium) since the use of the vaccine or serum.

May 20. Today 12 c.c. of rabbit serum were injected, this was followed by only slight local reaction, no fever. Pulse normal. Within two days two egg-sized nodes formed on the back of the left hand just below the wrist. These were not hemorrhagic, but slightly erythematous. The rheumatic symptoms of serum sickness followed. Her joints were so stiff that the patient could not walk. A peculiar accompaniment of the serum sickness in this case was the invariable stiffness of the neck muscles, anterior and posterior, with tenderness of the included muscles and hoarseness.

June 5. "Patient is now receiving the benefit of the last injection. The puffiness has all disappeared; there is no recurrence in the skin; old petechiæ are fading. The patient thinks the rabbit serum caused more stiffness and pain in the neck muscles than did the horse serum. She feels the same tonic effect which followed the previous injection after relief from the disagreeable erythema and joint symptoms (serum sickness)."

June 13. 5 c.c. rabbit serum injected without untoward symptoms following.

June 23. The patient is positive the last injection given June 13 has been productive of greater improvement than any of those preceding. There have been no new lesions since June 9.

From the time of the first injection, January 27, 1911, until October 6, 1911, eleven injections were given, all of which were of normal rabbit serum except the first two.

Besides the four above reported the following doses were given:

June 25, gave 7 c.c. rabbit serum.

July 12, gave 10 c.c. rabbit serum.

August 19, gave 5 c.c. rabbit serum.

September 6, gave 4 c.c. rabbit serum.

Two more injections, close together, were given between September 30 and October 6.

September 30. "Patient's general condition has improved materially and she has gained flesh, now weighs 136 pounds against 115. Has been able to go to Canada for a change, and during her stay there until the end of the month the purpuric symptoms gave her but little trouble."

The injection given October 6 was into the left arm, and was followed immediately by edema of the entire extremity, with the formation of enormous bullæ. Some of these were as large as an egg, tense, and filled with clear serum. There was no other reaction. The swelling extended to the axilla and the glands were enlarged. The bullæ were opened. In twenty-four to thirty-six hours the swelling subsided considerably, and the general condition of the patient improved.

October 13. Wherever there was a bleb there is a distinct hemorrhagic spot, deep red, nummular, corresponding in size with

the original bulla. Now there is no swelling of the arm, and the patient is thoroughly satisfied with the result of the treatment in spite of the annoying complication.

During the last year we have found that the injections of animal serum in this, as in cases reported by others, are better borne when given at short intervals within from ten to fifteen days, and we have therefore in our treatment of this case "bunched the injections" to the satisfaction of both the patient and the attendants, without serum sickness or symptoms due to anaphylaxis. Since October 11 the patient has received eight injections as follows:

October 14. Gave 2 c.c. fresh rabbit serum.

November 11. Gave $1\frac{1}{2}$ c.c. fresh rabbit serum.

December 16. Gave 1 c.c. rabbit serum.

February 10, 1912. Gave 0.6 c.c. fresh rabbit serum.

June 21. Gave 1 c.c. fresh rabbit serum.

June 28. Gave 1 c.c. fresh rabbit serum.

July 6. Gave $1\frac{1}{4}$ c.c. fresh rabbit serum.

July 13. Gave 1 c.c. fresh rabbit serum.

July 31. Made a blood count: White blood corpuscles, 7400; red blood corpuscles, 3,552,000; platelets, 1,136,000. The latter figure is about three times more than normal. We also find that the smaller doses given at short intervals control symptoms and have the tonic effect just as do the larger doses, without untoward complications.

In this case it may be said the animal serum has been given a long and fair trial. We are thoroughly convinced that its effect has been purely symptomatic and not curative. We are further convinced that besides its effect in controlling the hemorrhagic lesions between the injections the serum has had a decided tonic and exhilarating effect. We wish to emphasize the fact that this woman at the present time is still suffering from chronic purpura; that the pathogenesis of this as other cases is clouded; that there is an underlying constitutional disturbance, in all probability, which we have not unearthed; but the patient as well as her attendants realize the fact that we have at present no remedy which controls her symptoms so well as does the injection of the animal serum. As before, the slightest traumatism causes subcutaneous hemorrhage, which is likely to lead to superficial death of the included skin. There has been but a single physical sign added to those already given. During the months of June and July, 1912, in spite of a good general condition, the area of splenic dulness materially increased, and the organ itself was easily palpable below the free border of the ribs. The coagulation time of the blood has continued normal; the blood clot resulting has remained non-contractile; all these conditions are characteristic of the chronic types of the disease. The blood platelets have shown material increase.

October 18. Patient spent a comfortable summer on the coast of Maine; is without annoying symptoms; there are only occasional light colored purpuric spots, usually over the knees, symmetrical; and the spleen is no longer palpable.

CASE II.—Mrs. H. G. L., of Auburn, N. Y. Consultation with Dr. Woodruff June 27, 1911. Aged fifty-six years. Mother of two children; always feeble; fearful of cool air; always had a capricious appetite; "unable to eat as others do;" during entire life has been exceedingly hypersensitive. Passed the menopause at the age of forty-nine years without incident. Patient is an intelligent, nervous, well-developed woman. Family history clean, without taint, no suspicion of hemophilia or specific disease.

Previous History: Shortly before Dr. Woodruff first saw the patient, six years ago, she had practically starved herself; was feeble, and thought she needed "rectal treatment," which she finally received from three sources. One operator did "an extensive rectal operation," probably excision of a hemorrhoid and stretching of the sphincter; the second was called who "did something which made matters worse;" finally the patient found her way to Philadelphia, where she was successfully treated, and so far as her rectum is concerned she made a satisfactory recovery. For five years the patient has noticed "black and blue spots" on her body; they gave her no discomfort, coming and going, and were considered of no importance. Beginning with January, 1911, these were associated with marked symptoms of purpura, many of the earmarks of scorbutus, some of the larger hemorrhagic type. At times there was an admixture of purpura rheumatica, when she had severe pains in her legs and joints, with petechiæ covering the extremities and spots also on trunk, neck, and face, particularly about the eyelids, external canthi, and over malar bones. Toward the end of January, 1911, she commenced to show marked evidences of gingival purpura. The entire mucosa about the teeth became involved. This was spongy and purple; over and between each tooth when I first saw her the membrane was so swollen that "purple bags," as the intelligent nurse expressed it, "hung down and between the teeth." These looked like individual large blue grapes; made the patient uncomfortable, because of their size and tenderness; were so spongy and succulent they bled on the slightest touch. The nurse made the following note: "These swellings gradually extended around the whole mouth, looking like purple bags over each tooth. These were more tense just before they bled freely, after which the swelling subsided, but only temporarily." Ankles were swollen and tender.

For years the patient's digestion has been impaired. She feared to take food, as she could bear but little, and after several examinations of her stomach contents was told she was suffering from hyperacidity. Besides the gingival purpura at the time of my first

visit we found purpuric spots over her lower extremities; there were also "black and blue spots," which varied in size from a twenty-five-cent piece to macules which could scarcely be covered by the palm of the hand. These were tender and contained small palpable nodules of coagulated blood. Besides these large macules there were characteristic petechiæ, bright red pin-point to split-pea-size over the trunk and extremities, while here and there were remnants of former hemorrhages in pigment deposits. The patient had had severe epistaxis at varying intervals. At the time of our first consultation all of the cutaneous and gingival symptoms were at their height; the teeth could not be properly treated because of the tenderness of the gums. The stomach was intolerant and irritable, and the patient was unable to take sufficient nourishment, and had refused necessary food. She was obstinately constipated, and volunteered the information that she could never eat salt. She slept poorly.

Blood count: White blood corpuscles, 3800; red blood corpuscles, 4,700,000.

Differential count: Polymorphonuclears 71 per cent.; large mononuclears, 25 per cent.; small mononuclears, 4 per cent.

The coagulation time of the blood appeared to be normal, and there was no contraction of the coagulum. The arteries showed evidences of arteriosclerosis; the radial and popliteal arteries were abnormally tense and evenly thickened. The pulse in the dorsal pedal artery (left foot) was indistinctly felt. The area of cardiac dulness was slightly increased to the left; the impulse was heaving; there was a slight hemisystolic aortic murmur; the second aortic sound was accented; the mitral sounds were muffled; there was no distinct murmur in the mitral area. The area of liver dulness was slightly increased below the free border of the ribs. Systolic blood pressure, 160 mm. Hg.; diastolic pressure, 120 mm. Hg.; pulse pressure, 40. Repeated urinary analyses showed nothing abnormal, save that occasionally the specific gravity dropped to 1010, when the solid constituents were correspondingly lowered. Range of temperature, from 99° to 101°; pulse, 96; respirations, 20. Deep and superficial reflexes were all normal except the patella tendon reflexes, which were markedly exaggerated. The pains became so severe before the consultation that sedatives were needed "for comfort even during the daytime." She was bedridden at this time. After our consultation it was decided to insist on a rational diet, in spite of all objections and previous experiences, and to inject animal serum.

June 29. Injected 7 c.c. fresh rabbit serum (Meader) into the left mesogastric region. We quote from the nurse's report: "The night after the injection there was a slight redness around the spot of injection. The next morning the same surface was slightly mottled. The muscles were sore on that side of the patient's

abdomen, which she decided was the nervousness of changed conditions. *The pains in the legs ceased, so that she never after needed sedatives except two grains of veronal at bedtime; nothing during the day.* The purple spots began to fade and no new ones appeared except just under the left knee. Mrs. L. has become much interested in her case, and is trying to eat more, and now goes out-of-doors longer each day."

July 8. The patient has improved materially; is looking well, and eating better than before; ankles are neither swollen nor painful; there are only a few petechiæ; no new patches; gums are decidedly improved; do not bleed; are retracting; mucosa looks healthy. Injected 14 c.c. fresh rabbit serum today (Meader).

The nurse gave the following report: "The second treatment (injection) was given Saturday afternoon, July 8. In two hours Mrs. L. began to have 'nervous chills' in left hip and extending down the leg. The point of injection was sore at once. Patient slept well during the night following. The next day there was a red spot about the size of the palm of the hand around the injected spot, which itched considerably. This spot extended over the entire abdomen to the pubis. Temperature, 100°; pulse not materially disturbed. Flesh was hot and dry; felt uncomfortable; had severe headache and aching joints. Used lead and opium wash locally. At 9 P.M. began to perspire; pain ceased; temperature fell to normal, and patient slept well. For several days there was considerable dizziness when the head was moved. The skin and gum condition continued to improve, and the quantity of urine was increased to 2100 c.c.; some days, 2700 c.c. Patient helped herself better and was happier and encouraged."

July 18. "The purpuric symptoms are held in abeyance; improvement is continuous; suffers but little from gingivitis; the spongy condition of the gums has practically disappeared; no epistaxis; has no pains. Is eating well and takes a reasonable amount of nourishment. Temperature, 98°; pulse, 78; systolic blood pressure, 130. Urine free and normal."

July 24. Patient was found materially improved, and is looking much better. Gums retracted and look healthier. A few remnants of petechiæ left in the pigment deposit, and black and blue areas. On external surface of left ankle there is a long black and blue area. Feet are warm. Pulse in dorsal pedal artery distinctly felt. At 4.30 P.M. 17 c.c. rabbit serum injected (Meader).

It was after this injection that we had evidences of alarming anaphylaxis. Almost immediately after the injection the patient became drowsy. At 6 P.M. had a chill which lasted until almost 11.30 P.M. Considerable nausea. Had a desire to defecate (unsuccessful), and patient fainted and became cyanotic. Was returned to bed. Dr. Woodruff found her with weak pulse. She finally vomited a little. There was a continuous desire to go to stool. All these symptoms

correspond with those found in animals who are injected at long intervals, and are attributable to increased sensibility of the individual to the serum. Patient recovered fully in a few days from the effect of the injection, and the improvement in all symptoms was phenomenal.

August 14. Except a small ecchymotic spot on the plantar surface of the left foot and slight sponginess of the gums over the right upper canine there are no remnants of purpura.

October 4. Received 2 c.c. rabbit serum because of petechiæ on the legs. The gums are normal.

Blood count: Red blood corpuscles, 4,028,000; white blood corpuscles, 3600.

Differential count: Polymorphonuclears, 57 per cent.; small mononuclears, 29 per cent.; large mononuclears, 14 per cent.

No untoward symptoms followed this injection. Since November, 1911, there have been no evidences of a recurrence of chronic purpura.

Patient was thoroughly examined August 1, 1912, when the following note was made: "Has recovered completely from her chronic purpura, and has been without recurrence since last seen. She has normal mucous membranes; has gained in weight; color good; blood state good. Blood pressure, 140; respirations, 18; pulse, 76. Arteries slightly tense. Urine normal. Bowels constipated. For three or four weeks has had recurrence of burning sensation and points of tenderness in stomach region which she had many years ago. The burning is exceedingly annoying, and the nervous system is hypersensitive. The neurasthenic element is still in the ascendancy. Tongue clean."

Stomach analysis: Amount 50 c.c.; free hydrochloric acid, 40 per cent.; total acidity, 79 per cent.; lactic acid, very slight; blood, very slight; butyric acid, present; red blood corpuscles, few.

Microscopic examination: Starch granules; squamous epithelia. Her disagreeable stomach symptoms were controlled by belladonna and orthoform, with alkalies, and she is now (October 18, 1912) enjoying comparatively good health.

In the light of our recent experiences with these cases, and the knowledge gained by the study of the literature on the subject and animal experimentation, we would suggest in the future, to prevent annoying anaphylaxis, that similar cases be treated with injections of the serum during ten-day periods, the number of the injections to be given and the dosage to depend on a thorough study of the effect of a safe initial and second dose. The number of cycles of treatment should depend on the tendency of the individual case to relapse. Our second case, so far as evident symptoms of chronic purpura are concerned, in spite of its former chronicity during a period of six years, seems to be cured. It is unnecessary

to give the large doses which are suggested by some authors, one having given as high as 250 c.c. of fresh animal serum.³ In both of our cases the general improvement of the patients and increased weight almost immediately following treatment were satisfactory. Trembur⁴ has had similar experiences. The mental condition in both of our cases was improved. Case I expressed herself as follows: "The first and second days one aches all over and feels seasick; joints ache, and you feel just ugly and weak. There is a continuous desire to go to stool. After the fifth day you feel as if you had been given a great big tonic. The injection has an enormous effect on your mental state; it lifts you, and makes you feel better in all respects."

In "sporadic" hemophilia and acute purpura the results with animal serum are permanent, and we have had definite cures. In chronic purpura the prognosis, so far as permanent cure is concerned, is less favorable. The serum controls the symptoms in most cases, but it may be assumed from our present knowledge that the injections must be repeated. The serum of the bovidia is not recommended, because of the violent reactions which may follow its injection, including fever, rigors, cyanosis, and vomiting. Rabbit serum is recommended for all forms of hemorrhagic conditions requiring serum treatment; it is easily obtained by means of aseptic bleeding, and contains all the elements which are needed to control "dyscrasic hemorrhages." If necessary in an emergency, antidiphtheritic serum may be substituted until a fresh serum can be obtained. Recurring purpura with pernicious anemia is favorably influenced by the injections of animal serum, but in these cases there is always a strong tendency toward relapse. With chronic purpura and purpuric symptoms due to hereditary hemophilia the results from animal serum are at best temporary; repeated injections are necessary to control the hemorrhages and the massive types of visceral hemorrhages are controlled imperfectly. The greatest value of the treatment in these cases, according to Weil,⁵ is in the prophylactic injections of the serum before operative procedures are instituted. The results of treatment with animal serum are better in the type of hemophilia which Weil has characterized as "sporadic" or "accidental," in contradiction to the hereditary disease, a condition met in advanced life, accidentally encountered in normal individuals of both sexes. In these cases the blood reacts favorably to normal blood serum, and is thereby robbed of its hemophilic tendencies. The coagulability of the blood in these cases is favorably influenced by the serum, in the average cases

³ Pigot, *Gaz. Hebdomadaire de Med.*, October 17, 1897.

⁴ Serum Behandlung bei Hemophilie, *Mitteilungen aus den Grenzgebieten der Med. u. Chir.*, 1911, vol. xxii, p. 93.

⁵ L'Hemophilie, etc., *Presse Médicale*, October 18, 1905; *Tribune Médicale*, Paris, January 12 1907.

during three or four weeks. If such subjects demand surgical interference the most favorable time for operation is forty-eight hours after the injection. In chronic purpuras and hemophilics the serum may be given intravenously if such method of introduction is selected, with perfect safety, and without increase of hemorrhage, for the puncture of the vein in these subjects is promptly closed by its own elasticity, as has been repeatedly demonstrated by Weil.

The literature bearing on chronic purpura is meager and unsatisfactory, the classification of the purpuras offered by the French and German schools are also unsatisfactory; while our knowledge of the pathogenesis of many forms of purpura rests on an insecure and poorly constructed foundation. The cautious and continuous study of all types of chronic purpura makes positive the fact that the clinical picture is kaleidoscopic, and the cycles of the disease include repeated recurrences of all classified types of the disease in the individual case. In the chronic cases, with a simple purpura, there may be a prompt addition of the rheumatic form, and while this seems in the ascendancy, the hemorrhagic nature of the disease may be emphasized by drains from one or more mucous surfaces, occasionally hemorrhage into the brain or into hollow or solid viscera. Besides this our experiences justify the conclusion that chronic purpura may at times alternate with erythema multiforme, and included visceral symptoms, while in occasional cases, at times during their course, two or more types of purpura may be present and persist with varying intensity during limited periods at the same time.

In rare cases (one of which we have reported), whether because of embolic infarct, thrombosis, or necrobiosis, due to some other unknown pathologic cause, death of the infiltrated tissue results, corresponding with one or more of the original purpuric spots, all this in the presence of multiform hemorrhagic lesions, cutaneous, articular, and visceral. Immerman⁶ was in all probability correct when he contended that (1) simple purpura, (2) purpura rheumatica, Schoenlein's disease, (3) Henoch's purpura, involving skin, joints, and gastro-intestinal mucous membranes, and (4) purpura hæmorrhagica, or morbus maculosis Werlhof, are all identical, simply differing from each other in degree and intensity of constitutional symptoms. Chronic types of purpura may include, besides the hemorrhagic lesions, erythema, urticaria, and occasionally angioneurotic edema (Quincke's disease).

The histories of the cases of chronic purpura which have fallen under our observation prove them to be rebellious to ordinary treatment, and when influenced by treatment the periods of improvement by the older methods and drugs are exceedingly short,

⁶ Ziemssen's Cyclopedia.

for repeated relapse is likely to be the fate of all suffering from the disease. Thus one of the writers (Elsner) has seen cases covering a period of twelve and fourteen years respectively. Osler mentions a case which continued thirty-six years, and Halstead operated on a case of cancerous disease in which the patient had been purpuric since childhood.

Probably the most complete *resume* of our knowledge of chronic purpura with included histories of cases is from the pen of Bensaud and Rivet.⁷ These authors concluded that there is little mention in literature of the subject outside the common form known as Werlhof's disease. There are included references to articles mentioning 4 cases of the chronic form. These are (1) Rade, 1844, the case of a man, aged thirty years, who had two attacks in eight months; (2) Lancereaux, 1861, a chronic case, with large nasal and gingival hemorrhages, which finally died; (3) Lasegue, 1877, a case which appeared to be cured after three and a half months; (4) Denys, 1877, observed the case of a woman, aged forty years, who had successive attacks during two years. The article of Bensaud and Rivet further includes references to the researches of Hagen (1900), in which he emphasizes that the "chronic form is of certain frequency, and that it shows itself in successive attacks and remains apyretic." He reports several cases, and is more hopeful in his prognosis than our experiences would justify. One of his cases, a youth, aged eighteen years, had repeated attacks of purpura since his ninth year. Another, a woman, aged twenty-two years, had the disease since her seventh year. She had repeated epistaxis, and when aged eighteen years, commenced to have attacks of hemorrhagic purpura with her menstruation. One of his cases died in three months. A man, aged twenty-five years, had been purpuric since his tenth year, and finally had "hæmorrhagic periods," which were apyretic and characteristic of the chronic type of the disease in the multiform and varied lesions of purpura. Bensaud and Rivet further refer to a series of the chronic type in which, as in one of our reported cases, there were "periods of quiescence, during which the return to apparent health seemed complete, but the phenomena recurred on extreme fatigue." Their studies justify the following conclusions: Chronic purpura may present a variety of clinical pictures. There are two principal classes: (1) the continuous form, and (2) the intermittent form.

1. In the continuous form of the disease, patients present symptoms of general debility and rheumatism or of gastric or intestinal troubles. Both of our cases presented the latter. Examination of these patients shows ecchymoses or purpuric spots, which have been present for years, to which no importance has been attached because of their rapid disappearance. Epistaxis and

⁷ Archives Générale de Médecine, 1905, I. 24,

gingival hemorrhages are common in these cases. There are almost always some manifestations of purpura either on the skin or mucous membranes or some evidence of the hemorrhagic diathesis which is chronic and continuous, but without the great accidents which characterize the free crises of purpura hæmorrhagica.

2. The intermittent form of chronic purpura. This form appears to be more frequent. In these cases crises are separated by intervals of varying length. In the crises there are "abortive and anomalous phenomena." Crises are sometimes preceded for months or even years by frequent isolated hemorrhages, epistaxes, and stomatorrhagias. By themselves these crises are in no way distinguishable from Werlhof's disease. Contrary to current opinion these may be accompanied by febrile movement. After a variable length of time, often prolonged by the "subintractant attacks" so well known in the course of all purpuras, a latent phase follows when the patient appears cured. Until the appearance of a new crises there are no morbid phenomena. More often, if questioned carefully, however, some symptoms are mentioned; these include epistaxes, ecchymoses following the slightest traumatism or prick or menorrhagia suggesting uterine disease. At other times the general condition is disturbed; patients complain of stiffness; they frequently complain of digestive troubles; digestion is slow, painful, and accompanied by heaviness after meals; patients accommodate themselves to this condition until, as a result of influences not well determined, a new crisis follows, confirming the existence of the *chronic and intermittent* type of the disease. There are many clinical modifications. For instance, in three cases Bensaud and Rivet report a true alternation of mucous or visceral hemorrhagic crises with the purpuric eruption, which disappeared when the large hemorrhages appear, only to reappear quickly after them. A curious fact observed is that an intervening infectious disease (variola in one case, and erysipelas in another) does not assume a hemorrhagic character. In the cases studied by Bensaud and Rivet the duration was extremely variable. The long periods of quiescence in the intermittent form of the disease, and the further fact that most cases of chronic purpura are of this type, and the almost complete disappearance of subjective complaints during the periods are the reasons for the failure of many authors to recognize the existence of chronic purpura. Recurrences for more than twenty years were observed. Intermediary periods may be for a long period, as seven, eight, and in one case seventeen years.

Mode of termination is also variable. On account of the long latent periods it is never justifiable to conclude that the patient is cured. Patients may die during a crisis, so that one cannot call the disease benign. *Hemorrhage is the cardinal symptom of all types of chronic purpura.*

Diagnosis of chronic purpura is aided by the fact that the ma-

jority of observers are agreed that the blood clot does not contract, that the coagulation time is normal, and there is a belief among some that the blood platelets are diminished. This is not, however, uniformly true. The role which the blood platelets play in these cases and in the acute forms of the disease is now under consideration by the profession; it would seem that their presence in the blood is of great importance in aiding coagulation. This question will be more fully considered in the second part of this article.

The consideration of anaphylaxis in the use of animal serum is of the utmost importance, as the sensitization which may follow after the second injection or at any time during a series of injections may prove to be associated with serious symptoms, including sudden dyspnea, cyanosis, and in animal experimentation death has occurred. Fortunately this condition is rare in man. In both of our cases disagreeable symptoms have approached the more serious symptoms, which have resulted from animal experimentation in guinea-pigs. The method of treating these cases with small injections at short intervals during ten-day periods will in all probability prevent this disagreeable and annoying sequel. Auer, and Lewis and Auer⁸ have shown that atropin sulphate is a distinct protection against the asphyxia of immediate or acute anaphylaxis in the guinea-pig. These observations have been confirmed by others.⁹ The work of Karsner and Nutt¹⁰ on the relation of the intoxicating dose of Horse Serum to the Protective Dose of Atropin in Anaphylaxis in the Guinea-pig" gives some promise of success in its application to the human subject. At present there can be no objection to the administration of belladonna or atropin in small and safe doses following the second injection of the serum with the hope that a disagreeable and possible serious anaphylaxis may be prevented. Better still is the administration of the serum as suggested at short intervals during a limited period, preferably ten or twelve days, the thorough inquiry into the individual case to learn of possible idiosyncrasy or previous treatment with diphtheritic antitoxin. The consideration of anaphylaxis in connection with the treatment of hemorrhagic disease with animal serum will always claim the earnest attention of the therapist.

SERUM SICKNESS. In occasional cases, as in Case I, serum sickness may be annoying but not alarming. It may be associated with urticaria, arthralgia, and myalgia, but is evanescent. In

⁸ Acute Anaphylactic Death in Guinea-pigs, Jour. Amer. Med., 1909, liii, 458; The Prophylactic Action of Atropin in Immediate Anaphylaxis of Guinea-pigs, Amer. Jour. Phys., 1910, xxii, 439.

⁹ Anderson and Schultz, The Cause of Anaphylaxis and Some Methods of Alleviating It, Proc. Soc. Exper. Biol. and Med., 1910; A. Biedl and R. Kraus, Die Serum Anaphylaxie Beim Meerschweinchen, Wien klin. Wochenschrift, 1910, xxiii, 385.

¹⁰ Section on Pathology and Physiology, American Medical Association, 1911, p. 128.

spite of this disagreeable complication, purpuries are so much improved that they offer no objection to the repeated use of the serum.

THE RATIONALE OF THE SERUM TREATMENT OF HEMORRHAGIC DISEASES. Considerable literature has recently accumulated tending to show that the introduction of a foreign serum into the body of a patient afflicted with a hemorrhagic disease tends to bring about an improvement. The explanation for the phenomenon is at present not clear. However, a statement of facts in the case may be of interest, and perhaps lead to a clearer understanding of the problem involved.

Various explanations have been made as to the cause of hemorrhages, which may be briefly mentioned; abnormal thinness of the bloodvessel walls; abnormally high blood pressure; excessive amount of blood for the capacity of the bloodvessels; an inherited predisposition to a faulty structure of the cells of the body and blood; defects in the mechanism of coagulation, etc. In view of the fact that the coagulation of the blood in many of these patients seems to be delayed, it will be of interest to review the factors involved in coagulation.

There is present in the plasma a protein called fibrinogen. During the process of coagulation this protein is used up so that in blood serum which exudes from a blood clot its presence cannot be detected. The substance which unites with fibrinogen to form fibers of the clot is known as thrombin. It is not present in an active form in the blood plasma, but is formed soon after it escapes from the bloodvessels, and is present in the blood serum or the clot. Its formation is a complicated matter.

According to Howell there are two hypothetical substances existing in the blood plasma—antithrombin and prothrombin. When the latter unites with calcium salts thrombin is formed, but under the usual conditions in the bloodvessels the calcium salts are restrained from uniting with the prothrombin by the antithrombin, so that clotting in the vessels does not normally occur. When, however, blood is shed, thromboplastic substances from blood platelets and injured cells neutralize the antithrombin, so that the calcium salts are free to unite with the prothrombin and thus form thrombin. Thrombin unites with fibrinogen and forms fibrin—the essential part of a clot.

These two substances—fibrinogen and thrombin—are definite bodies. They can be isolated in a pure state and examined by the experimenter. Fibrinogen can be salted out of blood plasma or from the pathologic fluids of the body cavities, such as pleuritic fluid, hydrocele fluid, or ascitic fluid. A watery extract of thrombin may be made by appropriate means from blood serum, and if added to any of these abnormal body fluids above mentioned will bring about the immediate formation of a clot.

The point of special interest to us is the source of the thromboplastic substances above mentioned, which brings about the neutralization of antithrombin. Where do these substances, so-called cytozymes, come from? It was at first stated that they come from the leukocytes, but doubt is thrown on this source because leukocytes remain intact for a long time after being shed. They may be washed and may perform their normal phagocytic functions in the test-glass long after the clot has formed. More recently attention has been focused on the blood platelets. If the fresh shed blood is observed under the microscope these platelets are seen to agglutinate, and soon delicate fibrils are seen to radiate out from the masses of platelets. Methods have recently been devised for easily and accurately estimating the number of platelets per cubic millimeter of blood. The number for normal blood is placed at 250,000 to 400,000 c.mm.

The count of platelets in various blood diseases is interesting. Wright and Kinnicutt find that in secondary anemia the count is high, while in primary anemia the count is low. Duke finds that it is of value to differentiate coagulation time from bleeding time, that is, the time a wound will continue to bleed. He finds that in cases of prolonged bleeding time the blood-platelet count is low. He reports that a rabbit injected subcutaneously with diphtheria toxin, after a period of two weeks suddenly developed petechiæ and a prolonged bleeding time, which persisted for three days, and then disappeared. This disturbance was associated with a rapid decrease in the platelet content of the blood, and recovery followed their increase. He reports that in such diseases as idiopathic purpura hæmorrhagica, chronic ulcerative colitis, aplastic anemia, nephritis, the number of platelets is reduced, and that recovery is associated with their increase.

The blood platelets Wright believes come from the megakaryocytes of the bone-marrow. It is thought that they are short lived and are reproduced very rapidly, perhaps a sufficient amount to resupply the body can be made in four days. They are not found in defibrinated blood or blood serum.

Starling believes that the so-called blood platelets are not present in the blood plasma, but are substances, possibly precipitates, formed when the plasma touches a foreign surface. The constitution of these bodies or substances is immaterial so far as this discussion is concerned, since Starling attributes to them functions in the phenomenon of coagulation.

Having detailed to some extent the facts known to be associated with coagulation of the blood, let us return to our main problem and inquire farther why foreign and homologous serums appear to cause a patient to improve. It will be at once recognized that transfused blood will contain blood platelets intact, while homologous and foreign sera contain only the fragments or disinte-

gration products of these platelets, which are the real zymoplastic or thromboplastic substances; so that these bodies may be of service immediately in decreasing the bleeding and coagulation time. But, in addition to this, the injection of a serum into the body of an individual stimulates that body to the formation of antibodies.

Precipitins are formed and, further, the body becomes sensitized to this particular kind of serum. Using the nomenclature of von Pirquet, ergin is formed. Ergin is a hypothetical substance in the blood which is manufactured by the body cells for the purpose of digesting or protecting the body from a subsequent dose of the serum. During the process of digestion just mentioned a toxic body is liberated which produces the toxic symptoms.

Now it has been shown by Moss and Brown that the introduction of a foreign serum into a rabbit, whether sensitized or not, does not change permanently the relation between the kinds of leukocytes, but for a brief period after the injection there may be a marked relative increase of polynuclears, with a decrease of lymphocytes. The lymphocytes are manufactured in the lymph nodes, but the polynuclears are known to be made in the bone-marrow, where the megakaryocytes are located. Now may not the question be raised—Is not the physiologic change brought about by the immunization with a serum, an expression of unusual activity in the bone-marrow manifested by a shower of polynuclears and blood platelets, which latter improve the coagulating properties of the blood? In other words, are the blood platelets increased with immunization by a serum? Duke's work with transfusions suggest that they are, but so far as we know the question of increased platelets during immunization with a foreign serum is not answered.

An interesting recent observation in this connection is that of Duke's. He finds that when a large dose of a toxin (benzol or diphtheria toxin) is injected subcutaneously into a suitable animal a strong irritation is produced, and the platelet count decreases; while if small doses are given, a mild irritation is produced and the platelet count increases. In our cases above reported marked improvement followed the subcutaneous injection of small doses of rabbit serum, which may be explained by the supposition that a mild irritation is produced by the toxin liberated by the action of ergin, which irritation may have increased the platelets. This increase in platelets may increase the coagulating property of the blood. We have observed the blood platelets to be very numerous after a series of small doses of serum. This is accompanied by the clinical fact that the patient is much improved.

THE PRESENT VALUE OF THE WASSERMANN REACTION.

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IN recent years one of the greatest advances in medicine has been marked by the adoption of the Wassermann reaction in the diagnosis and treatment of syphilis. It has necessitated extensive revision of many of the older conceptions of the disease. The definite relationship of syphilis to the so-called parasyphilitic lesions has been established. Further, it has proved of immense service in the differentiation of doubtful cases, such as ulcers, growths, various bone diseases, etc. Greatest of all, however, its value in the treatment of syphilis has been abundantly demonstrated, as it has provided a method by which the success or failure of therapeutic measures can be determined.

Even at the present time, however, different authorities report considerable variations in the results of this reaction. Its technique is being almost continually modified, and the exact interpretation that can be placed on its application to the diagnosis and treatment of syphilis is not yet sufficiently definite.

Even for normal individuals the results are disputed, an average being from 0.3 to 1.2 per cent. of positive cases, although Noguchi reports as high as 3.6 per cent. These figures, of course, depend on the class of cases examined, as many who eventually show definite syphilitic lesions give no history of the earlier stages of the disease.

In the primary stage of syphilis the number of positive reactions varies in the reports of different authorities from 64 to 92 per cent. It is certain, however, that in most cases a positive reaction can be obtained by the end of the fourth week, so a definite diagnosis can generally be had a week or two before the appearance of the secondary eruption. In about 40 per cent. of cases the Wassermann reaction is positive when the initial sore appears, and the number of positive reactions becomes progressively more frequent until the development of the secondary eruption, at which time over 90 per cent. are positive. The earliest occurrence is reported by Lesser, who found a positive reaction as early as the eighth day after exposure. In this case the initial lesion appeared fourteen days later, and was followed six weeks afterward by a typical roseola. In my experience in about 9 per cent. of cases where no treatment has been received the reaction did not become positive until the first or second week after the development of the secondary eruption. Clinical evidences seem to show that with the development of a positive Wassermann reaction there is general systemic invasion of the syphilitic virus.

Experimentally, it has also been demonstrated by Neisser that with the development of a positive reaction the lymphatic glands and other tissues of the body become capable of transmitting the disease to apes. As a rule therefore there is systemic invasion of the virus some time before the development of the secondary eruption, and in a large percentage even before the development of the initial sore.

In secondary syphilis, positive results are reported from 80 to 100 per cent. Indeed, one may say that practically every untreated case gives a positive reaction in this stage, although its appearance may occasionally be delayed until one or two or even three weeks after the appearance of the secondary eruption.

In the tertiary stage, positive reactions are reported in 60 to 100 per cent. of cases, but more correctly in about 80 per cent. The figures in this stage of the disease, although they vary considerably, depend chiefly on whether the syphilitic process is active or healed. Almost every active tertiary lesion is associated with a positive reaction.

The most constant results are undoubtedly in secondary and hereditary syphilis. In congenital cases almost all give a positive result, even at birth (95 per cent. or over). That this is of practical importance is obvious, as many children after birth develop snuffles, and a positive Wassermann reaction both confirms the diagnosis and indicates that active treatment should be instituted at once. It also assists therefore in clearing up the diagnosis of stillbirth and habitual abortion. In 56 per cent. or more of apparently healthy women, the mothers of syphilitic children, there is a positive reaction. Similarly, the children of syphilitic mothers are not immune to syphilis, but, as can be shown by the Wassermann reaction, are either syphilitic or healthy, or may later become infected. Thus a woman having given birth to a syphilitic child, and having a positive reaction, is to be considered as having latent syphilis, and should be given specific treatment. Also a positive reaction in the child of a syphilitic mother, even though the child looks healthy, indicates that it also ought to be treated.

Pregnant women who have had a previous history of repeated abortions or stillbirths, and who are found to have a positive reaction, should be given antisyphilitic treatment, and in this way healthy children may be born.

In relation to the choice of wet-nurses, the importance of this reaction is obvious.

After the clinical signs of syphilis have disappeared, many cases, although apparently in good health, remain in a latent syphilitic condition. Reports in this phase of syphilis average about 65 per cent. of positive reactions in the early latent stage, and as many as 47 per cent. in the late stages. These figures are naturally subject to the widest variation; as the treatment of syphilis has

been so irregular in efficiency. Even in untreated cases it is difficult to estimate exactly how many will go on to a latent stage, and how long this may last, and whether it will lead to the late manifestations of syphilis, such as aneurysm, tabes, and paresis. By means of the Wassermann reaction the existence of latent syphilis may be recognized and adequate antisphyilitic treatment commenced. In this way the modern methods of treatment, which are guided by serum tests, have very materially lowered the percentage of cases of syphilis which have gone on to a latent stage, and so also of these latent cases which have eventually developed late syphilitic lesions.

In this latent stage of syphilis there may be no clinical manifestations which are obviously syphilitic, yet commonly such cases become extremely anemic, and often are the subjects of certain vague symptoms which usually disappear rapidly under anti-syphilitic treatment.

It is not uncommon to find cases, even when treatment has been fairly thorough, where the reaction remains positive for ten or fifteen years after infection, and cases are reported positive after forty years. Undoubtedly many such latent cases become spontaneously cured, yet all are liable to develop further manifestations of syphilis.

Reinfection with syphilis occasionally occurs, particularly in cases which have been satisfactorily treated; but so far as I know in no case presenting at the time a positive reaction. Certainly apes resist the development of syphilis so long as the serum reaction remains positive.

In the late manifestations of syphilis, such as the so-called parasyphilitic lesions, perhaps more than in any other relation, the Wassermann reaction is called on for discriminating diagnostic tests, and is also of special use in indicating the line of treatment which may arrest the progress of the disease. The importance of any reaction which can aid in distinguishing a gumma from other forms of cerebral tumor is undisputed. Thus, as a general rule, no case of operation for cerebral tumor should ever be undertaken without a negative Wassermann reaction, and in all cases of epilepsy starting in adult life this reaction is also suggested.

Tabes and general paresis are not then parasyphilitic, but metasyphilitic or truly syphilitic lesions. This does not mean that all cases of tabes are syphilitic in origin, as undoubtedly ergotism, anemia, pellagra, and a great variety of other conditions are associated with a moderate degree of degeneration of the posterior columns of the spinal cord, and consequently may present some symptoms of ataxia. The fully developed, progressive type of the disease is, however, definitely syphilitic. As a general average in paresis, 81 per cent. in the blood serum and 85 per cent. in the spinal fluid, and in tabes 65 per cent. in the blood serum

and 68 per cent. in the spinal fluid give positive results. In these cases it is the progressive types, with lymphocytosis in the spinal fluid, which furnish the positive reactions, while the stationary cases are generally negative. In cerebrospinal syphilis the reported results are rather conflicting, about 50 per cent. giving positive reactions in the blood serum and from none to 58 per cent. in the spinal fluid. It has been considered as a point of diagnostic importance that relatively few cases of cerebrospinal syphilis give positive reactions in the spinal fluid, yet when larger amounts of this fluid are used for the test, the positive reactions obtained closely follow the results in the blood serum. Cases of cerebrospinal syphilis usually give rather less frequent positive results than are found in tabes. Probably this is because many cases of cerebrospinal syphilis present only the results of the disease and not an actively syphilitic lesion. The examination of spinal fluid is valuable, as it gives very delicate reactions, although it does not seem to possess as much binding property as does the blood serum. It compensates for this, however, by not containing any complement, nor does it tend to develop anticomplementary actions in any way as extensively as occurs in blood serum. It therefore requires no devitalization, a process which considerably reduces the potency of the substances which produce a positive reaction.

It may well be wondered why any syphilitic infection can remain dormant in a spinal cord or other tissue and only after many years begin to produce its effect. Tubercle, however, may do the same thing, and some modifications in the subject's condition may be responsible for the sudden active development of the infective agent. Syphilis also may produce its effect slowly, and only after extensive damage are the lesions manifested clinically.

Other nervous diseases, such as amyotrophic lateral sclerosis, dementia præcox, disseminated sclerosis, syringomyelia, alcoholic psychosis, cerebral tumors, epilepsy, etc., are not related to syphilis, if one may judge by the negative reactions which they almost invariably present.

In diseases of the cardiovascular system, many questions at issue have been decided by this reaction. Cases of aneurysm, for instance, where the relation to syphilis has long been advocated, give positive reactions in about 70 per cent. of cases. It is also remarkable the frequency with which aortic incompetence is related to syphilis, as 72 per cent. are positive. Aortic incompetence in the majority of cases is syphilitic in origin, and therefore different in its etiology from mitral valve disease, in which the Wassermann reaction is generally negative. All other cardiovalvular lesions excepting aortic incompetence give only 24 per cent. of positive reactions. Even this latter figure undoubtedly shows the high incidence of cardiac disease in syphilis. Mesaortitis, or syphilitic

aortitis, occurs in about 82 per cent. of paretics, but in only 10 per cent of all syphilitics, and this therefore is as truly a parasymphilitic lesion as tabes or paresis. It is the essential lesion which is the precursor of most cases of aortic aneurysm, as only few of such aneurysms result from the ordinary form of arteriosclerosis.

Of all cases of arteriosclerosis only about 12 per cent. give positive reactions, showing that this disease may be produced by many other factors even as common or more commonly than by syphilis; and also that aneurysm in nearly every case has a syphilitic basis.

When we find it reported that in all cases of keratitis, exclusive of suppurative cases, 84 per cent., in iritis 38 per cent., in retinitis and in choroiditis 26 per cent., give positive reactions (Leber), the importance of this test in diseases of the eye is evident, particularly as an indication for therapeutic measures. Similarly it has been shown that ozena is generally, but not always, of syphilitic origin.

Before any application of the serum test for syphilis is made in relation to the diagnosis and treatment of the disease, the general biologic principles involved in the reaction, as well as the method of technique, must be thoroughly appreciated. It is essentially a laboratory method, and is only of value in the hands of trained serologists, as there are innumerable possibilities of faulty technique which may materially modify the result. It is not the comparatively simple process it was originally conceived to be, supposedly depending on the union of a definite syphilitic and antisyphilitic, antigen and antibody, mixture. The first antigens used were derived from syphilitic tissue, yet it has been shown that fatty extracts from normal tissues are capable of giving similar results.

One of the more common factors responsible for the discrepancies in the percentage of positive cases is variation in the quality of the antigen employed, and it is still a debatable point what variety of antigen is the most specific. It is undoubted that the use of a correctly standardized antigen, thoroughly tested for its specific properties, and which in comparatively large amount is neither hemolytic nor anticomplementary, will largely increase the efficiency of the test. In my own experience I have used watery and alcoholic extracts of syphilitic liver, as well as similar extracts of normal tissues; but have found that fatty extracts fractionated by alcohol, ether, and acetone, according to the method advised by Noguchi, gave materially the most reliable results. Such fractionated antigens made from syphilitic liver and normal ox heart seemed of practically equal value in giving specific reactions. Many authorities, however, obtain the best results with extracts of syphilitic tissue. Antigens, as a rule, retain their properties for a considerable time, but after several months tend to deteriorate and become less specific.

The reaction then seems to depend on the development in the

serum of syphilitic cases, of certain antilipoid substances, or, as has been suggested, of substances which have the power of destroying complement. It indicates, so far as can be determined, clinically and experimentally, an expression of the activity of the *Spirochæta pallida*, and is not therefore a true index of immunity against syphilis. The presence of antispiochete immune bodies can be determined by using an antigen made of spirochetes. The reactions obtained by lipid and spirochete antigens do not quite correspond, as the latter is much more limited in its range of positive reactions, almost none being obtained in the primary stage, and only rarely in the secondary. Positive reactions obtained with *pallida* antigens are particularly obtained in latent and tertiary syphilis. They seem to follow more closely the results of the cutaneous reactions produced byluetin, which is an emulsion of dead spirochetes.

Although by no means such a source of variation in the results reported by different workers, as might occur from many other details of the technique of this reaction, the merits of the several hemolytic systems have occasioned considerable dispute. The only systems in common use are the human, sheep, and ox, and each has its adherents. I have used all three, and found no great variation in the results. The most difficult reactions to interpret have been in the use of the human system, and with this indicator there have been more doubtful results than with either of the other systems. Even with careful washing of the corpuscles in preparing the hemolyticamboceptor, a certain amount of precipitation seems to occur with certain serums, which may considerably obscure the result.

With the sheep system a clear cut reaction is usually obtained, yet with this also there are certain difficulties. In my series of reactions over 90 per cent. of human sera contained some natural antisheep hemolyticamboceptor. About 35 per cent. contained between one and two units in 2 c.c. serum, and over 50 per cent. contained more than two units. Most varied between two and four units, yet some contained as many as seven, twelve, or even twenty units. Any marked excess of hemolyticamboceptor will in many cases convert a weak yet truly positive into a negative reaction. It is important therefore to recognize that in nearly half the cases the addition of extra artificial antisheep hemolyticamboceptor is unnecessary, and would tend to increase the number of negative results, as the requisite two units are already contained in the serum. By standardizing this natural antisheep hemolyticamboceptor, contained so frequently in human sera, and where it exceeds two units, if the further addition ofamboceptor be omitted about 9 per cent. more positive reactions will be obtained. These extra cases are those in which the specific agent in the serum was comparatively weak, yet they indicate definite evidence of syphilis,

as can be substantiated clinically and by doing a parallel series with an ox system. The delicacy of the sheep system may still further be improved by removing all the natural antisheep amboceptor from the human serum, by saturation with sheep corpuscles until all the hemolysis possible has occurred. By this means the possibility of negative results being produced by sera containing over two units of natural antisheep amboceptor may be avoided.

Perhaps the most reliable indicator is the ox system. This has been used by Browning, Peters, and others, but for some reason or other has never been very extensively adopted. It has, however, many advantages, as only 1 or 2 per cent. or practically no human sera possess any natural anti-ox hemolytic amboceptor. It also gives clear-cut reactions, and judging from its parallel use with the other systems, and the support of clinical evidence, is in my experience at least, the most specific. In the use of this ox system there is one factor which must be recognized, that ox corpuscles require a much longer period for sensitization with their corresponding amboceptor than do the sheep or human corpuscles. Incubation of the amboceptor and corpuscle mixture at 37° C. for half an hour, however, generally insures complete sensitization.

The standardization of the complement, the recognition and the removal of anticomplementary bodies in the human sera, besides numerous other details of technique, make this reaction one of extreme delicacy and reliability. Too often, however, it is conducted without a thorough appreciation of the numerous possibilities of error, and it is probable that variations in the method technique, as well as differences in the class of cases examined, have largely been responsible for the discrepancies reported in the results of the Wassermann reaction.

Although the biologic principles involved are still more or less unknown, yet clinical experience had practically established this reaction as a reliable indication of syphilitic infection. The severity of the systemic infection can also to some extent be gauged by the estimation of the degree of the positive character of the reaction. If efficiently conducted it is almost specific, only very few other diseases being associated with positive reactions, and these irregularly. Cases of leprosy are credited with between 10 and 70 per cent. of positive reactions. Noguchi found it positive in 72.4 per cent. My own experience is limited to three cases, all of which were negative. In scarlet fever, also, reports vary extensively from 1 to 50 per cent., Swift finding 5 per cent. and Fua and Koch 12 per cent. In yaws and trypanosomias the Wassermann reaction is also described as frequently positive, so also in some occasional cases of anemia, tuberculosis, cancer, lymphadenoma, leukemia, etc. Since the discovery of the reaction, improvements in technique have,

however, greatly improved the specificity of the reaction, and considerably fewer positive reactions are now obtained in other diseases than syphilis, so that for all practical purposes the finding of a positive reaction indicates a diagnosis of syphilis.

The value of a negative report, although important, is not quite so definite. A positive reaction may occasionally be delayed until the second week of the secondary stage. The disease may be the result of syphilis, yet exist in a healed condition where there is no spirochete activity. Occasionally also in some acutely syphilitic cases the serum may be negative, as if the spirochetes were not sufficiently active to produce a positive reaction. In such cases the diagnosis of syphilis does not have to stand on the report of the Wassermann reaction alone. A negative reaction may also be the result of recent treatment. Also the binding substances in the serum may be in such small amounts that the preliminary devitalization of the serum reduces them until they are insufficient to produce a positive reaction. Such weak reactions are commonly encountered in the late stages of treatment. Negative reactions may also be readily produced by imperfect technique.

As the greater certainty of the Wassermann reaction in its technique and specific relationship to syphilis has become more thoroughly established, the treatment of syphilis is now largely guided by the results of the serum tests, a positive reaction being held as indicating the presence of active spirochetes in the body. It has provided a method of making a certain diagnosis of syphilis in a much earlier stage than was formerly possible. Efficient treatment can therefore be commenced much sooner, when the disease is more readily influenced, and also with the natural result of lessening the possibility of future development of tertiary syphilitic lesions. Some few cases still seem to resist the most active treatment and develop tertiary lesions. Yet with the methods of treatment at present adopted, tertiary, latent, or late syphilitic manifestations should be eliminated. Certainly the longer the commencement of treatment is delayed the greater difficulty will be experienced in permanently removing a positive reaction from the serum, and until this is done the patient cannot be pronounced cured. It can be shown that even minute traces of mercuric bichloride can destroy the binding substance in a syphilitic serum, *in vitro*. It is therefore not to be wondered at that even after short courses of treatment the number of positive reactions is greatly reduced. One negative result is then of little importance, especially if it occurs in course of treatment. If treatment is stopped the activity of the spirochetes recommences and a positive result can again be obtained. Repeated negative results, however, at intervals after the cessation of the treatment, indicate the probability of a final cure. A serum should not be examined for the Wassermann reaction before one month after

the cessation of treatment, as negative results before this are of little importance. A negative result six months after the termination of the course of treatment would seem to indicate a cure. If, however, the reaction has again become positive an entire new course of treatment must be instituted. In latent cases, in which the reaction is recognized as positive some years after syphilis has been acquired, the treatment often has to be very vigorous and prolonged before the serum becomes permanently negative. An interesting finding, and one which is sometimes of use in doubtful cases, is that after an injection of salvarsan in a recently treated syphilitic presenting a negative reaction the serum may again become positive for a short time, as if the drug temporarily stirred up the activity of the spirochetes in the tissues. The time after which treatment causes the reaction in the serum of a syphilitic case to become negative varies with the severity of the case, the stage of the disease, and the extent of treatment. Sometimes two or three doses of mercury cause a temporary disappearance of the binding substance in the serum. In others very extensive treatment has to be pursued before the reaction becomes negative. The result of experimental and clinical experience seems to warrant the assumption that the appearance of a positive reaction in the serum is coincident with a systemic syphilitic infection. It indicates that treatment should be actively pursued, even though the subject is apparently in good health. It has therefore given a method by which a large percentage of the serious after-results of syphilis, such as aneurysm, aortic incompetence, tabes, paresis, keratitis, and the birth of syphilitic children, may be prevented.

Even if any such untoward results have occurred, there is now a considerable amount of evidence that their progressive character may be arrested by antisyphilitic treatment. Such damage to the bloodvessels as occurs in aneurysm or to the nervous system in tabes and paresis is of course permanent, but if the progression of these diseases can be stopped, then a great advance has been marked in their treatment. Also in the case of tabes, the undamaged portions of the cord may assume a considerable proportion of the functions which have been impaired by destruction of certain tracts. Thus reëducation exercises may largely improve the clinical condition of the subjects of this disease after its progressive character has been arrested. That some cases of late syphilis present negative reactions it is also of importance to recognize, as it prevents the indiscriminate administration of antisyphilitic treatment when the disease is already stationary and a healed process, and in which specific treatment would be of no avail.

The study of the Wassermann reaction in the last few years has shown that by the older methods of treating syphilis only in about one case in four was this successful.

Some cases were undoubtedly cured, in others treatment was

unnecessarily prolonged, but in the majority the infection persisted and if the disease was not eventually eradicated by natural means, then late syphilitic manifestations were liable to occur.

The serum diagnosis of syphilis has demonstrated the inefficiency of mercurial treatment by internal administration. It has led to the discovery of the great tolerance which the intestine may acquire to this drug, so that after a time its only effect is to impair the nutrition of the patient. As Fordyce has stated: "Day after day we see patients the victims of paresis, tabes, etc., all giving identical therapeutic history of having had internal mercurial treatment for two or three years. The method stands condemned by its eloquent results."

It has shown the efficiency of treatment by salvarsan and neo-salvarsan and also that combined with hypodermic injections of mercury salts; it is better than either alone. Although the hypodermic administration of mercurial preparations is greatly superior to internal treatment and may cause a very rapid disappearance of the external evidences of syphilis, yet only very slowly and often uncertainly, does it effect a cure, as judged by the frequent persistence of positive serum reactions.

With the aid of the Wassermann reaction syphilitic cases can be managed so that there is the least danger of relapses or the development of complications. It has therefore been one of the most important factors in the adoption of the present, earlier commenced, more rapidly effective, more certain, and more scientific methods of treatment.

DIAPHRAGMATIC HERNIA, WITH REPORT OF A CASE.

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INTEREST in diaphragmatic hernia has been greatly stimulated since the recognition of the condition has been so much facilitated by the development of Röntgen-ray technique. Although the lesion is not a remarkably rare one, until recently the diagnosis had but seldom been made, owing to the difficulty of correctly interpreting its physical signs. Grosser,¹ for example, in 1899, was able to collect records of 433 cases, but Arnsperger² makes the statement that up to 1908 the condition had been recognized during life in not more than 10 instances. Now, however, by

¹ Wien. klin. Woch., 1899, No. 24, p. 655.

² Deutsch. Arch. f. klin. Med., 1908, xciii, 88.

means of radiography, intrathoracic conditions can be studied much more effectively, and it is possible not only to determine the presence of a diaphragmatic hernia with certainty, but in many instances to ascertain its exact nature. It is probable that the condition is much commoner than the number of published cases would lead one to suppose, for frequently, as in the case of the patient forming the subject of the present report, hernias of even the most extreme type give rise to no subjective symptoms and are revealed only as postmortem surprises should an autopsy be performed for some other reason.

True diaphragmatic hernias, like those involving other portions of the abdominal parietes, consist of protrusions of abdominal viscera through congenital or acquired openings. The definition requires the presence of a sac, composed in this instance of a layer of peritoneum and one of pleura. Such protrusions, through the diaphragm, can take place either when one of the preformed foramina is abnormally wide from birth or gradually becomes so, or when, owing to deficiency or weakness of the muscle bundles, a weak spot exists through which the abdominal viscera can force themselves. This process is, of course, facilitated through the state of latent negative pressure constantly existing in the thorax. Accordingly, such protrusions of peritoneum forming a sac and passing through a hernial ring in an uninjured diaphragm are termed diaphragmatic hernias. It has been customary, however, to speak also of diaphragmatic hernia in those cases in which abdominal organs have entered the thorax through an actual aperture in the diaphragm, either natural or traumatic in nature. Under these conditions no real sac exists and the invading structures are free in the chest cavity, but the clinical manifestations are essentially similar and the term "false hernia" is applied. Diaphragmatic hernias may also be classified as congenital or acquired, and, finally, it is necessary to consider a condition clinically resembling a hernia and known as diaphragmatic eventration. In this, one-half of the diaphragm becomes greatly relaxed, so that the abdominal organs encroach upon the thoracic cavity and a hernia is simulated. The diaphragm remains intact, however, and there is no sac or hernial ring. Before discussing the symptomatology and diagnosis of these various conditions it will be well to go a little more into detail regarding the separate forms.

1. *False Congenital Diaphragmatic Hernia.* This is by far the commonest of all the diaphragmatic hernias, and according to Liepman³ forms 87 per cent. of the congenital hernias. It results from imperfect development of the diaphragm, so that an opening of greater or less size permitting free communication between the thoracic and abdominal cavities exists from birth. In one case

³ Arch. f. Geburtshülfe, 1903, lxxiii, 780.

reported by Klebs (Eppinger⁴) the diaphragm was totally absent, yet the child lived to the sixth year. Usually, however, the defect is much less extensive, and it is commonly situated on the left side. The opening is most often found in the space between the costal and lumbar portions of the diaphragm. Gössnitz⁵ has shown by studies in comparative anatomy that this area is developmentally the last portion of the diaphragm to be closed, and he found that small defects invariably occur in this situation. The larger the opening, the greater is the involvement of the lateral and, finally, of the ventral areas of the costal portion of the diaphragm. In extreme cases almost the entire left half of the diaphragm may be missing, only a vestige of muscle extending from the sternum laterally to the chest wall. The various grades of congenital defect, therefore, may be regarded as different degrees of arrested development. Occasionally, however, defects originating in the sternal portion are seen, and the occurrence of several small sharply circumscribed openings in situations bearing no relation to the development or the anatomical structure of the organ has also been described.

The influences which are operative during intra-uterine life in impeding the normal closure of the diaphragm are not clear, and of the various theories advanced that of Laterjet and Jaricot⁶ is perhaps the most plausible. They point out that the portion of the diaphragm that is the last to close is the most poorly vascularized, and that a slight degree of abnormal pressure here would suffice to cause nutritional disturbances leading to an arrest of development. The fact that the right side is almost never involved—Dietlen and Knierim,⁷ in 1910, reported the first case of right-sided defect diagnosed during life—lends color to the belief that the presence of the liver may serve in some sense as a protective agency in preventing disturbances of development.

2. *True Congenital Diaphragmatic Hernia.* This requires that a complete closure of the septum transversum shall have taken place, so that a true hernial sac is formed with a layer of peritoneum on the one side and one of pleura on the other. In other words, a congenital arrest of development occurring at a later period than in the preceding group leads to a thoracic protrusion of the most recently closed and, therefore, weakest portion of the membrane, before there has been a growth of muscle sufficient to resist the pressure. The sac is usually very large, invading a considerable portion of the thoracic cavity, and most often contains stomach and intestine, sometimes even portions of liver and pancreas.

⁴ Allgemeine und specielle Pathologie des Zwerchfells. Supplemente zu H. Nothnagel's Spezielle Pathologie und Therapie. Wien und Leipzig, 1911. (Contains an elaborate chapter on diaphragmatic hernia and extensive bibliography.)

⁵ Inaug. Dissert., Jena, 1903.

⁶ Bibliographie anat., 1909, xviii, 22.

⁷ Berl. klin. Woch., 1910, No. 25, p. 1174.

3. *True Acquired Diaphragmatic Hernia.* This consists of a protrusion of peritoneum through a hernial ring, which is formed either by the dilatation of one of the natural foramina, or, very rarely, by the giving way of a circumscribed weakened area acquired after birth. Hernias have been observed through Larrey's sternocostal space, through the triangular space described by Bochdalek, bounded by the outer lumbar crus, the adjoining costal portion, and the last rib, through the esophageal foramen, and through the opening for the sympathetic trunk. No hernia has yet been described as occurring through the aortic opening or that for the vena cava.

4. *Acquired Perforations of the Diaphragm* result not in true hernias but in a prolapse of abdominal viscera into the thorax, and so give rise to false traumatic hernias. They may be produced in two ways: either by penetrating stab or gunshot wounds, or by blunt violence causing rupture of the diaphragm. Of these, the former is far commoner; thus Iselin⁸ found that of 90 cases 76 were due to stab wounds. The course in such cases is varied: death may follow in consequence of other complications, or closure of the opening through adhesions to neighboring organs may take place. Spontaneous closure of the opening is unlikely and the non-fatal cases usually end in chronic traumatic false hernia. The prognosis of operative closure by suture is good. Rupture of the diaphragm without external wounds may be caused by such injuries as being run over, falls from a height, crushing accidents, railroad buffer accidents, etc. Here again the left side is most affected, the proportion varying according to different authors from 15 to 1 to 4 to 1. Bell⁹ has reported a case of long standing in which a nodule of liver with a constricted neck was found projecting through an old rent in the diaphragm apparently not due to an external perforating trauma.

In a third small group of cases rupture has been caused by violent vomiting. An instance of this is described by Daxenberger,¹⁰ in which a man, aged twenty-three years, died sixteen hours after a violent vomiting attack. At the autopsy the stomach was found greatly dilated, owing to an old cicatricial stenosis of the pylorus, and was prolapsed through a fresh rent in the diaphragm. Perforation of the diaphragm due to suppurative processes such as subphrenic abscess, empyema, suppurative pericarditis, etc., seldom leads to hernia owing to the adhesions always present.

5. *True Atypical Traumatic Hernia.* This is a rare type, in which there is a true hernial sac, but the ring is not situated at one of the physiological openings. The protrusion takes place through a weakened spot in the diaphragm, which must still be covered

⁸ Deutsch. Zeitschr. f. Chir., 1907, No. 88, p. 150.

⁹ AMER. JOUR. MED. SCI., 1909, cxxxvii, 581.

¹⁰ Münch. med. Woch., 1906, No. 7, p. 313.

with peritoneum. Schlatter,¹¹ in 1901, reported a case in which a stab only partly perforated the diaphragm and a hernia followed. Engel, Lukseh, and Cruveilhier (Eppinger¹²) have described somewhat similar cases.

6. *Diaphragmatic Eventration, or Diffuse Relaxation of the Diaphragm.* This is not a hernia at all, but the differential diagnosis is often so difficult that the condition must be considered with the hernias. The relaxation of the diaphragm may be so extreme that its dome-shaped summit reaches the level of the second rib. It is practically always left-sided, and in 1910, Dietlen and Knierim¹³ said that no instance of right-sided eventration had ever been reported, but Eppinger¹⁴ has since then performed an autopsy on such a case. In consequence of the enormous dilatation the diaphragm naturally loses its muscular quality and becomes converted into a fibrous membrane, with occasional muscle bundles streaking inward from the periphery.

Although Laennec appears to have seen a case of this lesion, and it was Petit who gave it its name early in the last century, only 20 cases have been reported. Its pathogenesis is obscure and most authors assume a congenital predisposition, associated in some cases with degenerative changes in the muscle fibers. The liver seems to act as a protective barrier in preventing the occurrence of the relaxation on the right side. Partial relaxations involving only a portion of the left side of the diaphragm have also been described as diaphragmatic diverticula.

From what has been said it follows that the various lesions described may be classified as follows:

I. True hernias: (A) True congenital hernias in which pleura and peritoneum form the sac and only the muscular or tendinous layer of the diaphragm is absent. (B) True acquired hernias. (a) True typical acquired hernias with the ring originating at one of the natural foramina. (b) True atypical acquired hernias with the ring developing in a situation other than at one of the natural foramina.

II. False hernias: (A) Congenital false hernia through a congenital defect. (B) Acquired false hernia due to traumatic perforation of the diaphragm and either acute or chronic

III. Diaphragmatic eventration due to relaxation of the diaphragm and either involving an entire half of the diaphragm or localized in the form of a diverticulum.

DIAGNOSIS. It is almost inconceivable that extreme dislocation of organs that like the stomach and intestine are undergoing constant alterations in size can exist for years without giving rise to any subjective disturbances, yet such is the case and in many

¹¹ Münch. med. Woch., 1901, No. 48, p. 34.

¹² Loc. cit.

¹³ Loc. cit.

¹⁴ Loc. cit.

of the instances reported the abnormality has been revealed only at the autopsy. This, of course, is true especially of the congenital defects, which frequently give rise to symptoms only late in life, often as the result of apparently negligible inciting causes. Instances have been described in which the previously unsuspected condition was made manifest after dancing, exertion, exposure, or loss of flesh, but on the other hand, some of the patients have never been free from symptoms. Petit's patient, for example, died at the age of forty years after a history of constant attacks of vomiting, dyspnea, and pain, one of which finally ended fatally.

The physical signs in cases in which the hernia is large are usually significant and often conclusive. On the other hand, if the sac is small and centrally placed the diagnosis may be very difficult. The displacement of the heart to the right is very common and should always lead to the suspicion of some form of diaphragmatic hernia if the more usual causes of dextrocardia can be excluded. Since the hernial contents are always largely made up of stomach and intestine tympany can be elicited where normally there should be pulmonary resonance. The area over which it is heard varies at different times, or on changes of position in accordance with the variations in the amount or level of the contained fluid. The breath sounds are absent except at the edges of the area where the lung is in contact with hollow viscera and here there may be a metallic or amphoric quality to the respiratory murmur. Frequently gurgling sounds are present, similar to those heard on auscultating the abdomen. Succussion may be obtained at times, but it is characteristic of this as of other physical signs that it depends on the condition of distention with gas or fluid of the organs at the time of examination. Respiratory changes in the line of pulmonary resonance at the base behind, and Litten's diaphragm phenomenon may or may not be present depending on the mobility of what remains of the diaphragm. The affected side of the thorax is usually larger, the intercostal spaces are filled out, and there may even be respiratory protrusion between the ribs, especially in children. The patients frequently cannot lie on the healthy side because of the resulting cardiac distress, which as well as dyspnea and cyanosis may be brought on by very slight exertion. The abdomen may or may not be retracted, and if the spleen forms part of the protrusion its area of dullness will, of course, be absent. The stomach cannot be located in its usual situation by the customary methods of inflation, etc., and the sharp kinking of the esophagus makes the introduction of the stomach tube difficult or impossible. The same condition gives rise to the so-called dysphagia paradoxa, sometimes present, which consists in the fact that large masses of food are swallowed more readily than small well-chewed mouthfuls which cannot so well be pushed along by the distended esophagus. The dis-

placed stomach usually swings about completely so that its greater curvature is uppermost, but there is great variability in the degree of the subjective gastric disturbance. Frequently a sensation of fulness and oppression in the thorax is complained of after eating.

Hematemesis is a common symptom, and may be due to congestion, incarceration, or ulcer. The thoracic dislocation of the colon may be ascertained by the changes in the physical signs following inflation or the administration of high enemas. Constipation is a common symptom.

Parasternal hernia is the commonest of the true hernias and occurs most often in stout middle-aged persons owing to the invasion of Larrey's space by adipose tissue. A significant sign of the lesion is a gurgling sound heard over the sternum synchronously with the heart beats. There may be a tympanitic quality to the percussion note in the same situation. Paraesophageal hernia is often accompanied by dysphagia, and the introduction of bougies into the stomach may be painful, difficult, or impossible. Eppinger¹⁵ speaks of a ringing musical murmur accompanying the first heart sound as an important sign.

The most important feature in the examination is, of course, the use of the Röntgen ray, but it is necessary to make many examinations, at different times, in different positions, from different angles, and with and without the use of bismuth. Some authors, like Hirsch,¹⁶ have found the pictures obtained after the introduction of a mercury-filled stomach tube especially significant. Giffin¹⁷ emphasizes the obliteration of the distinctly dome-like outline of the normal diaphragm. Eventration and hernia through a large congenital defect, while anatomically totally different conditions, may clinically resemble each other so closely as to make the differential diagnosis extremely difficult or impossible. All the recent writers emphasize the value of radiography in distinguishing between the two. In eventration the shadow of the distended diaphragm is to be seen as a delicate line arching across the summit of the protruded mass of viscera, an appearance that is lacking in cases of hernia. Beltz¹⁸ suggests that in difficult cases it may be possible to make the diaphragm shadow visible separately by slowly filling the stomach with air in different positions. A differential sign to which some authors attach importance is that if there is a defect of large size there is inspiratory elevation of the prolapsed viscera, while in eventration the fluoroscope shows an appearance approaching the normal inspiratory descent of the diaphragm. With the same idea in view, Hess and Jannin¹⁹ suggest observing on the fluoroscope the effect

¹⁵ Loc. cit.

¹⁷ *Annals of Surgery*, March, 1912.

¹⁹ *Deutsch. med. Woch.*, 1906, No. 49, p. 1990; *Verhandl. d. Kongr. f. innere Med.*, 1906, p. 359.

¹⁶ *Münch. med. Woch.*, 1900, No. 29, p. 996.

¹⁸ *Münch. med. Woch.*, 1910, No. 19, p. 1006.

of electrically stimulating the phrenic nerve, but adhesions between the viscera and diaphragm may make even this test unreliable. Eppinger,²⁰ indeed, comes to the conclusion that there is no single sign that can be accepted as positive evidence of eventration.

In the differential diagnosis such conditions as pneumothorax, subphrenic abscess, subphrenic pyopneumothorax, and esophageal diverticulum must be thought of and eliminated.

In spite of the usually large size of the ring, incarceration occurs in 15 per cent. of the cases. It is brought on by such conditions as torsion of the viscera, the taking of large quantities of food or fluids, increased intra-abdominal pressure caused by vomiting, straining at stool, or parturition, falls or abdominal contusions, etc. Or adhesions may form about the prolapsed viscera so that peristalsis is interfered with, giving rise to pain or other symptoms, and perhaps eventually to incarceration. Volvulus of the herniated intestine has also been known to occur. The symptoms are those usually seen in cases of incarceration at other hernial openings. If they appear in those previously suspected of having a diaphragmatic hernia, the diagnosis of hernia is confirmed, but when, as is sometimes the case, the incarceration is the first sign of any anomaly it may be a matter of much difficulty to ascertain the site of the lesion. Displacement of the heart to the right may give a clue, and the pain is said to be characteristic in that it extends through the chest with its point of maximum intensity below the hypochondrium, and is increased in inspiration. Girdle pain and dysphagia are sometimes observed. The intestinal obstruction may lead to distention of the abdomen or thorax, the latter, of course, being very significant. Dysphagia and hematemesis are common. Some patients give a history of numerous slight attacks of incarceration; others die of shock in the first attack, or from peritonitis following gangrene of the strangulated viscera.

It is difficult to be definite in speaking of the prognosis other than to say that in general it is that of all hernias, for even in cases in which there are no symptoms the menace of incarceration is always present. On the other hand the discovery at autopsy of a diaphragmatic hernia in an individual who never experienced any discomfort from the abnormality shows that in a certain number of cases the outlook is perfectly favorable. Patients in whom the existence of the condition is ascertained should be told of its nature and be warned of the possibility of incarceration. Eppinger²¹ makes the suggestion that some generally understood symbol should be branded on the abdomen of such persons to serve as an indication to the surgeon who might at some future date be confronted with the puzzling picture of incarceration. In eventration the prospects are better, but even here intestinal obstruction may follow. In the traumatic cases the prognosis, of course, depends

²⁰ Loc. cit.

²¹ Loc. cit.

on the severity of the associated injuries, but any wound of the diaphragm, even if apparently not attended by immediately serious consequences, must be regarded as a matter of great gravity owing to the danger of subsequent incarceration.

As far as treatment is concerned it may be stated of the traumatic hernias that as soon as the existence of a fresh wound of the diaphragm is ascertained immediate operation is indicated. The very prompt prolapse of the abdominal viscera makes spontaneous closure of the opening almost impossible. Isclin²² found in 90 cases of operation for traumatic hernia collected from the literature that in 56 cases omentum or an abdominal organ presented in the external wound; and in 6 further cases abdominal contents were found in the thorax on opening the chest. In 64 left-sided cases there was omentum in the external wound 44 times, and 5 times in the pleural cavity, and in 5 instances stomach or intestine presented. In only 10 cases was there no prolapse. Prolapse of the omentum is especially important as it appears to be the first structure to enter the wound and then acts as a guide for the colon and stomach, thus favoring their prolapse. In a recent contribution Magula²³ from a study of 190 cases emphasizes the importance of immediate exploration in all cases of perforating wounds of the lower thorax or upper abdomen in order that a possible opening in the diaphragm may be promptly dealt with.

The prognosis is good when a prompt operation is performed, and according to Isclin the mortality depends only on the degree of injury to the gastro-intestinal tract. In non-operative cases the external wound may close and the patient apparently recover, but it is almost inevitable that sooner or later, often after years of freedom from symptoms, a hernia will develop. In operating most authors prefer the transthoracic route as affording better access to the wound in the diaphragm, but, on the other hand, while suture of the opening is more difficult from the abdomen, Isclin²⁴ points out that when approached from this side injuries to the stomach or intestine are less likely to be overlooked. In some cases the diaphragm was first sutured by enlarging the thoracic wound, and the abdomen then inspected through a laparotomy. The perils of pneumothorax are not considered grave, and at present can be rendered negligible by resort to one of the recent methods of differential pressure. Eppinger²⁵ found in 1911 that in 115 cases subjected to operation there were 17 deaths; that is, 14.7 per cent. Suter²⁶ in 1905, gave the mortality as 13.8 per cent., Isclin in 1907, as 16.6 per cent. Death in most cases was due to injuries to the stomach or intestine. In the sutured cases no subsequent hernia has been observed. In 6 cases of rupture of the

²² Loc. cit.

²³ Loc. cit.

²⁶ Bruns' Beiträge, 1905, No. 46, part 2.

²³ Arch. f. klin. Chir., 1910, xciii, 581.

²⁵ Loc. cit.

diaphragm operated on, only 1 recovery was obtained, the deaths being due to the severity of the trauma or to infection.

In chronic hernias the treatment is entirely directed to the prophylaxis of incarceration by restricting the amounts of food and fluids taken at a time; anything likely to bring on vomiting must be avoided, constipation be guarded against, and pregnancy be prevented. Surgery is indicated only in case incarceration occurs. In cases developing shortly after a trauma the thoracic route is preferable, but in long-standing cases it is better to operate from the abdominal side as it is then easier to separate adhesions about the lower surface of the hernial opening. Carson and Huelsman,²⁷ however, have recently described a successful operation on a congenital hernia in which the seventh, eighth, and ninth ribs were resected.

The following case is a striking example of an extreme instance of congenital diaphragmatic hernia existing without subjective symptoms, death resulting from an independent lesion. The patient was admitted for a surgical condition in January, 1912, to the service of Dr. Abbe, at St. Luke's Hospital, to whom I am indebted for the opportunity of examining the bedside notes. The patient was a Scotchman, salesman, aged forty-seven years, who came to the hospital suffering from abdominal pain and other symptoms referable to a stenosis of the large intestine, with attending peritonitis, which ended fatally. The history included no symptoms that could be connected with the astonishing dislocation of the abdominal viscera which was revealed at the autopsy.

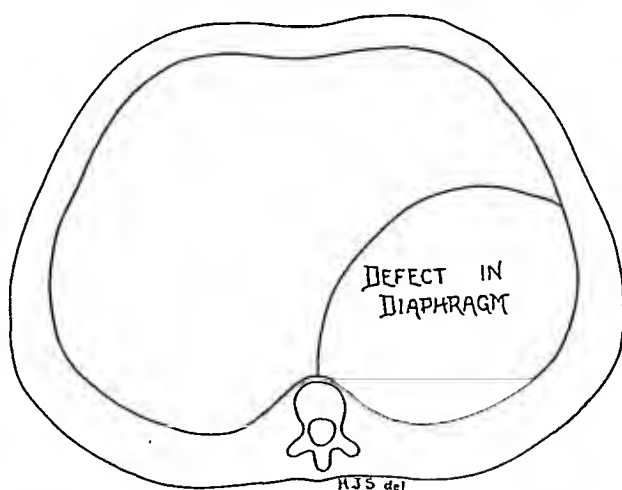


FIG. 1.—Diagram of the diaphragm seen from below, showing position and relative size of the defect.

AUTOPSY. The accompanying illustrations clearly indicate the relations of the displaced organs. On opening the thorax the

²⁷ Interstate Medical Journal, April, 1912.

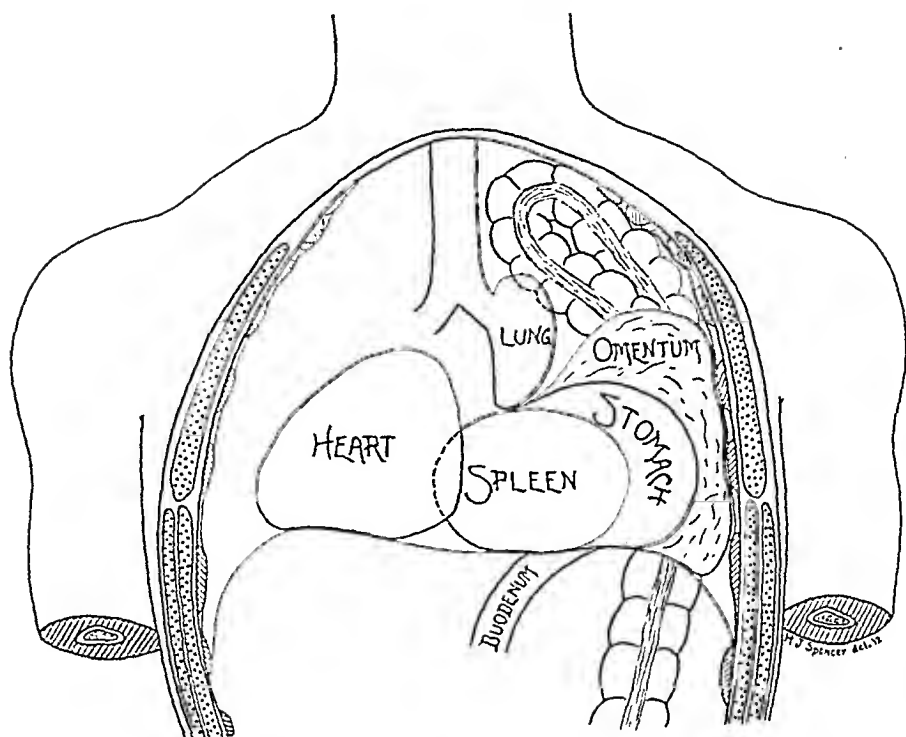


FIG. 2.—Diagram showing relations of the viscera as seen on opening the thorax.

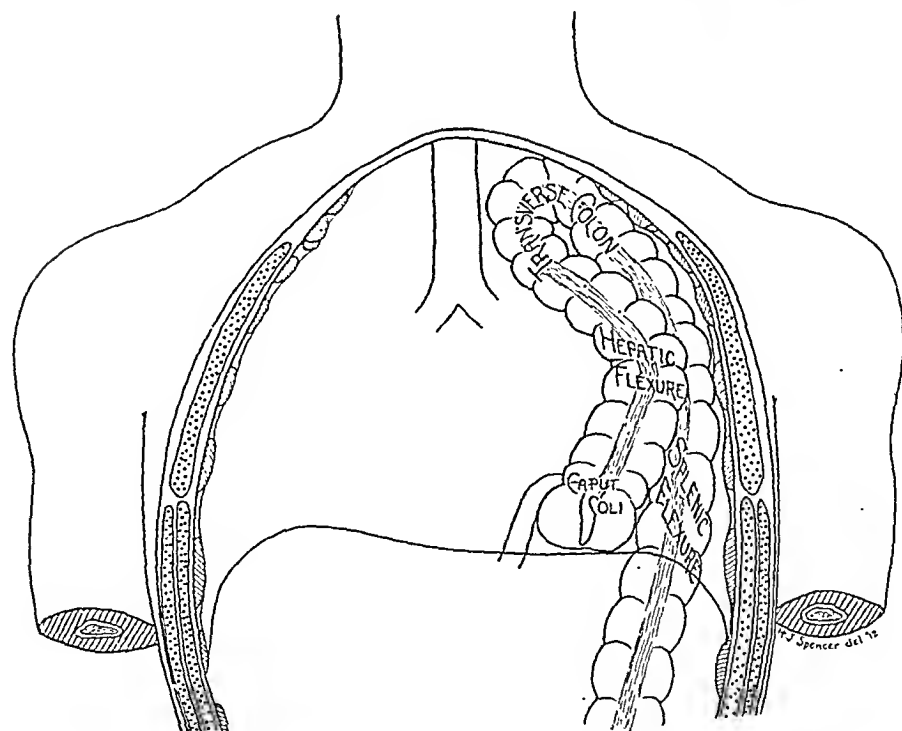


FIG. 3.—Diagram showing the general arrangement of the greatly distended coils of large intestine.

colon was seen occupying the left chest through a left-sided diaphragmatic defect. The spleen weighed 180 grams and was about in the position of the heart. The left lung was collapsed and measured 14 cm. in length, 7 cm. in width, and 2 cm. in thickness. The right lung presented numerous firm adhesions to the chest wall, but was otherwise normal. The left border of the heart was 2.5 cm. to the right of the median line, the right border, 11.5 cm. to the right of the median line, the upper border at the third rib, the apex at the sixth rib, 1.5 cm. inside the mammary line. The left



FIG. 4.—Photograph of the portion of the sigmoid stenosed as the result of diverticulitis, with the mouth of the largest pocket shown at A.

chest was filled with omentum, caput coli, transverse and descending colon; a few inches of the ileum were lying above the diaphragm. The descending colon was straight and ran directly to the brim of the pelvis. The gut was much distended. The omentum was adherent to the transverse colon, making a sort of bag, but was not in any way adherent to the chest wall. The stomach lay above the diaphragm with the duodenum passing through the opening. The hernia could be easily reduced. The hernial opening occupied the posterior and lateral portions of the diaphragm, was about 15

cm. in diameter, and had rounded and somewhat thickened edges. A loop of small intestine was adherent to the sigmoid at the brim of the pelvis. The sigmoid was constricted for a distance of 5 cm., so that even the little finger would not pass through the obstruction. The muscle was thickened above the constriction. The mucosa was practically normal except for four

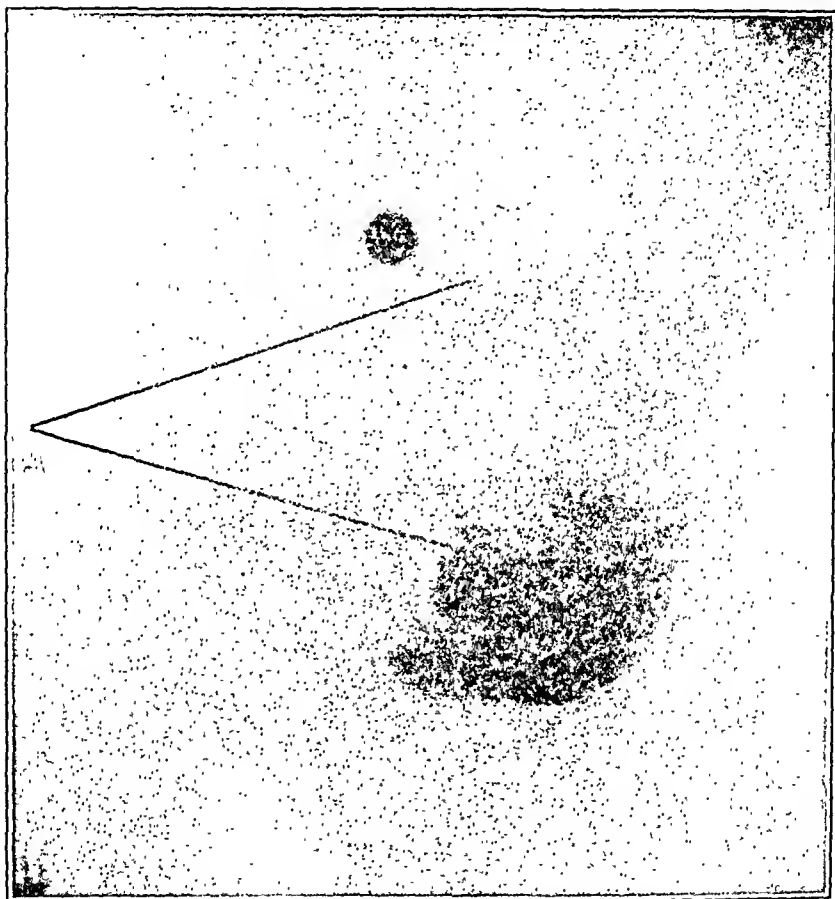


FIG. 5.—Bismuth radiograph showing at A the portion of the sigmoid stenosed as the result of diverticulitis.

pockets with mouths 0.5 cm. in diameter. These pockets varied in depth from a few millimeters to several centimeters. There was a thick collar of firm inflammatory tissue some 12 cm. long about the sigmoid just above the pelvic brim, binding the gut down to the posterior abdominal wall. There was a band of fat and inflammatory tissue over the surface of the sigmoid, aiding in the constriction. The other organs presented no abnormalities.

DIAGNOSIS: Perisigmoid inflammation (diverticulitis) with obstruction and beginning peritonitis. False congenital diaphragmatic hernia.

CONCLUSIONS. Diaphragmatic hernia is much commoner than generally supposed, and may exist indefinitely without giving rise to symptoms. Dextrocardia and physical signs suggesting those of pneumothorax should always cause the possibility of this condition to be thought of and lead to careful radiographic study of the thorax.

SOME CONSIDERATIONS REGARDING THE FACTOR OF FATIGUE, WITH REFERENCE TO INDUSTRIAL CONDITIONS.¹

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WITHIN the past few years considerable literature has grown up with reference to the general subject of fatigue, and more recently it has been sought to utilize the results from the investigation of fatigue in helping to solve some of the industrial and occupational problems. While the mass of literature about these subjects is so large as to make any effort toward reviewing it at this time a practical impossibility, yet from it all there stand out certain general principles to which it is well worth while to call attention. There are certain other fairly well-accepted facts which belong within this same sphere, but which as yet have not received the recognition which is their due, to which attention also may be invited.

In the first place the problem of fatigue has been most thoroughly worked over with reference to the subject of muscular fatigue and with the use of the nerve-muscle apparatus. Here the problem has been a relatively simple one, and yet even with all its simplicity there remains a variety of questions to be answered, and the undisputed conclusions are few. It is generally admitted, as a result of this kind of work, that fatigue has two factors, a negative and a positive: the former the result of an actual wearing out of the used substance, in this case muscle, and the second the result of the formation of certain poisonous substances such as carbon dioxide, paralactic acid, and monopotassium phosphate. The term exhaustion has been proposed for this negative side of fatigue, while the word fatigue itself is used solely by some authors to indicate the positive side.

These results are results of the fatigue of muscle. The question of the fatigue of the nervous system is an entirely different one. As soon as an effort was made to define the actual place where

¹ Read at the International Congress of Hygiene and Demography, Washington, D. C., September 23, 1912.

fatigue occurred in the living animal or the nerve muscle apparatus it was found to be no easy matter. In general, however, it may be said that the nerves themselves do not fatigue, and that the conception of the central nervous organs themselves showing fatigue, as is more particularly set forth by the experiments of Hodge, has changed materially of late years until it is now believed that the central nervous organs, like the nerves themselves, are little susceptible to fatigue. In the case of the nerve-muscle apparatus it would seem as if the nervous tissues were saved from fatigue by the fatigue of the muscle, or that both muscle and central nerve organs are saved from fatigue by fatigue of the motor end plates in the same way that a dynamo may be saved from damage by the melting of a fuse. The classical experiment of Sherrington, which was to the effect that a muscle which is connected with a spinal cord centre, which centre may be reached by several afferent tracts, responds as quickly to stimulation through one of these afferent tracts after one of the others has been so exhausted that no results follow its stimulation, indicates that the locale of the exhaustion is at the synapse between the afferent and efferent neuron, and that, again, the central nervous organs are protected from exhaustion by this synaptic exhaustion just as in the former case they were protected by motor end-plate exhaustion. If these are the mechanisms, then it is readily seen that neither the nerves nor the central nervous system itself can ever be seriously exhausted, that the synaptic junctions and the motor end plates interpose obstacles to the occurrence of any serious disintegrating processes, and therefore are protective devices for conserving the organism.

At this point one cannot resist drawing certain analogies. We have seen that it is fairly well conceded that the motor end plates and the synaptic junctions, by becoming impervious, prevent exhaustion of the central nervous system; so it is commonly accepted that in the mental sphere disorder of attention has the same conservative function. The person who can no longer pay attention is saved from the possibilities of serious exhaustion, and this conclusion is in harmony with the more recent belief, *contra* the original opinions following the experiments of Hodge, that the central nervous organs really do not suffer from exhaustion.

Again, mental fatigue is still more complex. We have no knowledge at all for correlating the symptoms of mental fatigue with any definite changes in the nervous system, and our means of measuring mental fatigue are most of them so complex when one comes to investigate them, and so contaminated by other than mental factors, that it is extremely difficult, in fact almost impossible, to evaluate the results. It is obvious, for example, that such instruments as the ergograph or the dynamometer, the esthesiometer, and the algometer all involve both mental and

physical factors, while when we come to take up the question of the symptoms of mental fatigue, we realize that defect of attention is one of them. Then when we realize that the whole attitude of psychology toward attention has been materially changing of recent years, and that attention is being more and more considered as an affective state, as an affective orientation of the individual as a whole toward a stimulus in the environment, the muscles naturally playing a large part, it becomes evident that the difficulties are certainly very great. In the face of these difficulties it would seem that we had better stick to fundamental principles and not mix our categories and so not endeavor to speak of fatigue in one category in terms of fatigue in another. Let the mental and the physical, or as symptoms, called the psychic and the physiologic, remain apart, and endeavor to determine questions of fatigue in the mental sphere purely in mental terms. For this purpose probably the best method is Kraepelin's method of continuous additions.

This much I have said preliminarily because questions of fatigue which arise in the consideration of industrial and occupational problems almost invariably imply fatigue both of mind and of body. It will be seen, thus, that in speaking of fatigue we are using a term of vague connotations, and dealing with a condition that admits of measurement only with the greatest of difficulty. Not only this, but in the present state of our knowledge it is practically impossible to state wherein the fatigue is resident, what part of the individual really is fatigued, and what are the mechanisms both chemical and physical of that fatigue. The general gross fact which seems to issue from this complex situation is that human beings, worked under given conditions, tend to show a gradual falling off in the efficiency of their work, and that this falling off in efficiency can be prevented by changing the conditions, more particularly by increasing the opportunities for rest; and that, further, when human beings continue to work under conditions which show a gradual falling off in efficiency, other manifestations tend to come into evidence—namely, various kinds and descriptions of disturbances of health. So that with our present knowledge it would seem more accurate, and perhaps wiser, to deal with the human being as if he were a machine and with his efficiency as measured by his output and endeavor to find what the conditions are which lower his efficiency, either impairing it temporarily or tending to impair it permanently, and then endeavoring to discover what the conditions are which will prevent this temporary or permanent impairment, and so increase the efficiency.

I have been tempted to say what I have said, which is more especially a plea for greater definiteness in the use of terms, by looking through the literature of fatigue, particularly in connection with various occupations, and noticing with what little regard

for accuracy the term fatigue and certain other terms are used. I refer more particularly to the conditions which are presumed to be the results of mental fatigue. I find numerous papers, some of them by talented writers, showing the prevalence and the increase of neurasthenia and hysteria in certain occupations; and I note the statistics, especially those of foreign sanatoria for the working classes, showing the immense increase in cases of nervous diseases that were admitted to these sanatoria during recent years. There appears to be little in any of this literature that at all adequately accounts for these conditions.

In the realm of the neuroses and the psychoneuroses, such particularly as neurasthenia and hysteria, to which I have called attention, the particular character of the work or its severity could by no possibility operate as adequate causes if our present ideas of these conditions are correct. Hysteria, for example, is a mental disease, dependent upon purely mental causes, in other words, psychogenic in origin. Work of any character, description, or degree of severity could not be conceived to be a cause in any true sense. It is well known that if we have some weak point in our bodies it bothers us more when we are not in good condition, and we are able to adjust ourselves to it better when we are in good health. The muscles of accommodation, for example, partake of the tone of the general musculature, and when health is good they may give little trouble, but when health is poor, they may cause difficulty. In the same way, and only in that way, can occupation or fatigue of any kind be said to be a causative factor of hysteria. It can only be an adjuvant cause at best, and at that, you will see, an unimportant one. With neurasthenia we are dealing with a condition which is not so prominently mental. In fact, neurasthenia, as we understand it today, is not a mental disorder at all, but a physical disorder. However, the term neurasthenia is perhaps one of the most loosely used terms in medicine, and as I see it through the literature that I have spoken of before, there appears to be no definiteness about its use. It is applied to all sorts and conditions of things, including the whole realm of the neuroses and the psychoneuroses, and probably some of the actual insanities. We have a fairly well-defined syndrome to which the term neurasthenia is applicable, the symptoms of which are, in the main, a feeling of pressure on the top of the head, more or less insomnia, spinal irritation with perhaps pain in the back, certain paresthesias, easy fatigability, and emotional irritability. This may be a primary neurosis or it may be a secondary one following upon other illnesses, such as prolonged sickness of some kind, or succeeding an acute illness, such as typhoid fever. As a primary neurosis it may be described as a primary fatigue neurosis, although it must be realized that the assumption that it is due to fatigue and that the symptoms

are dependent upon the elaboration of toxic fatigue substances is purely hypothetical. Even admitting the truth of all these things, however, there is absolutely no warrant, if our present concepts of this condition are correct, and they are being verified every day, for believing that occupation of any kind or of any degree of severity can be other than a purely adjuvant and unimportant cause of this condition, as is the case in hysteria.

The limits of this paper prevent any extensive illustration of the opinions that I have just brought out with reference to hysteria and neurasthenia. It will be recognized that I have in mind the more recent hypotheses of Prof. Freud, who would place both of these diseases, and a number of others, in the same category—namely, he would ascribe as the necessary etiological factor in both cases some sort of disturbance in the sex life of the individual, so that these diseases become of great importance, not only because they are, as I would call them, social diseases, but because their problems are essentially broader than the individual—they are biological problems. A single illustration will give an idea of how I regard the situation.

It will be seen in the literature, for example, that many of the telephone girls are becoming neurasthenic, and the cause is attributed to long hours of work, the extreme effort of attention that is necessary because of the character of the work, and its constant annoyance and irritating character. All these things are true, but if the modern hypothesis of neurasthenia, to which I have referred, is correct, they cannot be the fundamental causes. To speak broadly we can only understand the neurasthenia in such cases by thinking of these girls as individuals who have been prepared by nature, up to a certain point, to fulfil a certain function; and then because of the exigencies of life, all the energies which have been developed in that direction are, so to speak, side-tracked, and at about the period of puberty, when nature might expect physiological fulfilment, the individual is called upon to make a complete readjustment, to find entirely new avenues of outlet for nervous energy, to concentrate upon entirely alien interests. Some people are so constituted that they can do this thing; as a result they succeed. Others are so constituted that they cannot. They become neurasthenic or develop other neuroses, while certain others, and they are perhaps the most frequent, occupy a borderland position. These girls under favorable conditions of employment, with plenty of opportunity for rest, good food, good housing, etc., manage to get along. With prolonged hours of work and irritating conditions, perhaps coupled with unhygienic and unsanitary living, they break down. So it will be seen what is meant by fundamental causes, and how we regard the usually attributed causes as only adjuvant. It will be seen also why we believe the problem is deeper than the individual, and strikes at once at the

social conditions brought about by the various industries and occupations.

We might speak of other conditions, but these two are sufficiently illustrative. Hysteria surely and in all probability neurasthenia belong to the diseases which are not dependent upon the introduction into or the action on the body of some specific morbid agent. They are essentially social diseases which depend for their existence upon the maladjustment of individuals to their social surroundings, their inability to meet the demands that are made upon them because of their relations to other people, actually or prospectively, and as such these diseases cannot be dependent for their existence upon long hours of work or upon the character of that work. These considerations, however, do not make it any the less important that these conditions be considered in connection with the various industries, nor do they make it obvious why there has been such an increase in the number of these diseases. A moment's reflection will convince anyone that their importance lies not in the fact of their association with any particular kind or character of work so far as the fatiguing qualities of that work may be concerned, but in the fact that they are expressions of causes that are more widely operative, social causes which have invaded and changed the social conditions under which people live, and evidently changed these conditions disadvantageously, so as to make possible the outcropping of these diseases, and investigation of industrial conditions should realize this factor in the situation as exemplified by the presence of this class of diseases.

My plea, then, in this paper is for the recognition of what we have termed social diseases, for a realization that the problem of the various industries, as that problem deals with the question of the health of the workers, is a broader problem than the problem of ordinary physical disease. It is a problem which touches the whole question of society, and which presents for consideration the neuroses and the psychoneuroses as indications of a disease which is not individual, but social. Here we have in this class of diseases a point of attack upon abnormal social conditions, and by their study some kind of idea may be had as to the best means of approaching the faulty social conditions of which they are the expression, and which may be incident to the industrial conditions under consideration.

The necessary restrictions of such a paper as this make it impossible for me to illustrate what I mean except briefly. It has been shown by careful analysis of certain cases of these psychoneuroses that the disorder was dependent upon experiences in the early years of childhood—types of experiences which, in many instances, were dependent upon the general crowded condition in which the families were forced to live. It will be seen, therefore, in such cases that the disorder from which the patient suffers

leads directly back to social conditions, which social conditions may or may not be dependent upon industrial conditions. The psychoneuroses, therefore, may become a good barometer of certain social states dependent upon industrial conditions, and while it is known that the social state of the worker has been investigated fully, still we do not think that it has been appreciated that many of the specific manifestations of illness are outward indications of certain types of social conditions that are undesirable. It will be seen then that a correlation between the work of the psychiatrist and neurologist and the social worker is possible along these lines. This paper merely bespeaks a recognition of the advantage of this correlation, which if pursued would be seen to offer many possibilities for work.

THE TOPOGRAPHY OF THE CARDIAC VALVES AS REVEALED BY THE X-RAYS.¹

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For many years attempts have been made to determine definitely the exact spots on the anterior chest wall under which lie the valves of the heart. The method by which studies in this direction have been made has consisted of the thrusting of long pins into the thorax and then opening the latter and noting the points at which the pins pierced the heart. From data thus obtained diagrams were constructed which were supposed to depict the valves in their relation to the anterior chest wall. That this method is inaccurate is demonstrated rather forcibly by the lack of unanimity in the descriptions given by various authors. In the following excerpts we present the opinions of a number of authorities, and it is interesting to note that the more superficially located is the valve the more nearly do the different authors agree, while the deeper lies the valve the more widely do the writers disagree.

¹ Read before the College of Physicians of Philadelphia, October 2, 1912.

Aortic: Behind the junction of the third left costal cartilage with the sternum, one-fourth covered by pulmonary valves. *Pulmonary*: Behind the upper border of the third left costal cartilage and the adjacent part of the second left intercostal space. *Tricuspid*: Behind the left half of the sternum at the fifth costal cartilage and the fourth intercostal space. *Mitral*: Behind the left half of the sternum at the third intercostal space and at the fourth intercostal space.²



FIG. 1.—In this x-ray photograph every valve is shown with great clearness. On account of cardiac hypertrophy and sinistro-displacement, all the valves lie well to the left of the sternum. P, pulmonary valve; A, aortic valve; M, mitral valve; T, tricuspid valve.

Aortic: Behind the sternal end of the third left intercostal space. *Pulmonary*: A little above and behind the third left chondrosternal junction. *Tricuspid*: Behind the middle of the sternum at the fourth intercostal space. *Mitral*: Behind the fourth costal cartilage at the left border of the sternum.³

² G. A. Gibson, *Diseases of the Heart and Aorta*, 1898, p. 38.

³ John B. Deaver, *Surgical Anatomy*, 1903, p. 409.

Aortic: Slightly below and internal to the pulmonary on the level with the third space between the midsternal and the left sternal line. *Pulmonary*: Behind the sternal end of the third left costal cartilage. *Tricuspid*: On the horizontal line between the two sternal ends of the fifth cartilage at the point intersected by a line drawn from the sternal end of the third left cartilage to the upper border of the sternal end of the seventh on the right. *Mitral*: Behind the sternal end of the third left space.⁴

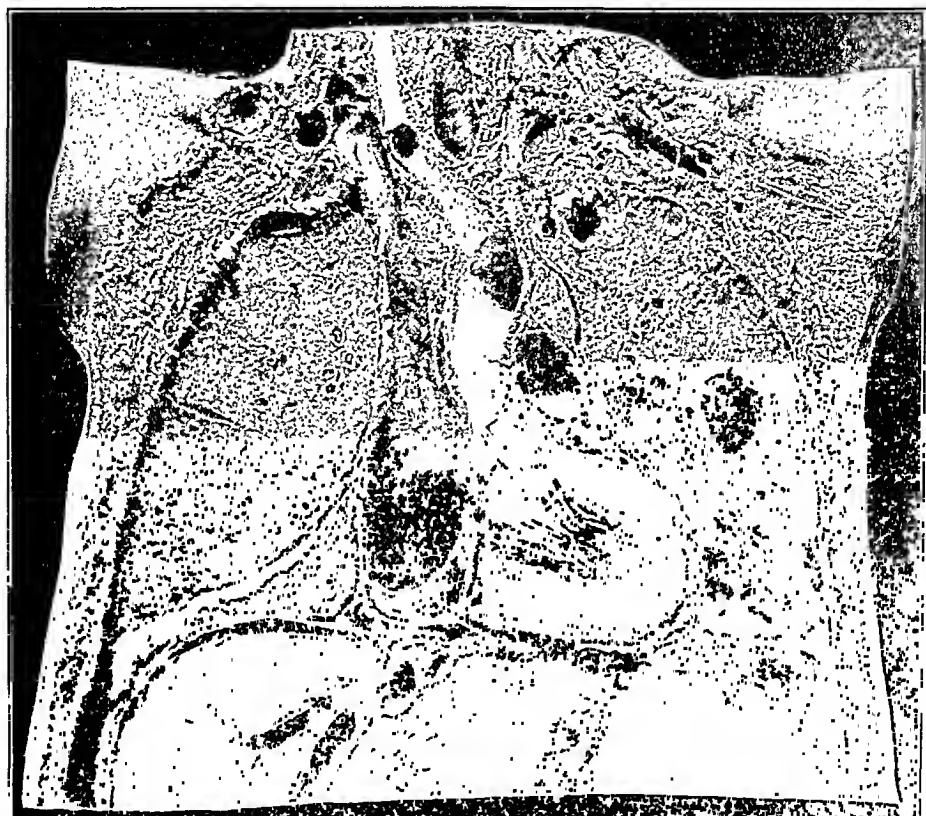


FIG. 2.—Frontal section of the thorax, the x-ray picture of which is shown in Fig. 3. The tuberculous cavities of the left lung are well shown in the x-ray plate.

Aortic: Lower border of the third left costosternal junction. *Pulmonary*: Upper border of the third left costosternal junction. *Tricuspid*: Just to the left of the midsternal line level with the fourth space. *Mitral*: Fourth left costosternal junction.⁵

Aortic: The third left intercostal space. *Pulmonary*: Third left costosternal junction. *Tricuspid*: Midsternum at the level of the fifth costosternal junction. *Mitral*: Fourth left costosternal junction.⁶

⁴ de Nancrède, *Essentials of Anatomy*, 1911, p. 183.

⁵ Henry Gray, *Anatomy*, Philadelphia, 1908, p. 559.

⁶ C. Toldt, *Atlas of Human Anatomy*, New York, 1904, Part 5, p. 586.

Aortic: Lower border of the third left costosternal junction. *Pulmonary*: Upper border of the third left costal cartilage close to the sternum. *Tricuspid*: Behind the sternum at the level of the fourth interspace and anterior extremity of the fifth costal cartilage extending down to the right almost as far as the sixth chondrosternal junction. *Mitral*: Behind the left half sternum at the level of the fourth chondrosternal junction.⁷



FIG. 3.—X-ray photograph of thorax, a frontal section of which is shown in Fig. 2. Of the cardiac valves only the semilunars show with clearness. The tuberculous cavities of the left lung and the internal mammary vessels are well demonstrated. *P*, pulmonary valve; *A*, aortic valve.

Aortic: Opposite the inner lower border of the third left costal cartilage. *Pulmonary*: Upper border of the third left costal cartilage at its sternal junction. *Tricuspid*: Behind the sternum from the opposite fourth left interspace to the fifth right interspace. *Mitral*: Left edge of the sternum at the level of the fourth left costal cartilage.⁸

Aortic: Behind the third intercostal space, close to the left side of the sternum. *Pulmonary*: In front of the aortic valve,

⁷ L. B. Rawlings, *Landmarks and Surface Markings of the Human Body*, London, 1908, p. 37.

⁸ C. R. Whittaker, *Essentials of Surface Anatomy*, London, 1912, p. 29.

behind the third left chondrosternal junction. *Tricuspid*: Behind the middle of the sternum, about the level of the fourth costal cartilage. *Mitral*: Behind the third intercostal space, about one inch to the left of the sternum.⁹

Aortic: Middle of the sternum, at the level of the third costal cartilage. *Pulmonary*: Second intercostal space, somewhat to the left of the edge of the sternum. *Tricuspid*: Midway between



FIG. 4.—Frontal section of the thorax, the x-ray picture of which is shown in Fig. 5. There should be noted the cut surfaces of the aorta, the pulmonary artery, and the left auricular appendix, all of which appear clearly in Fig. 5.

the third left and the fifth right chondrosternal articulation. *Mitral*: Beneath the third left chondrosternal articulation.¹⁰

Aortic: Behind the left half of the sternum at the lower border of the third costal cartilage. *Pulmonary*: At the upper border of the third left chondrosternal articulation. *Tricuspid*: From the midsternum at the level of the fourth costal cartilage to the

⁹ John H. Musser, *Medical Diagnosis*, 1900, p. 595.

¹⁰ Herman Sahli, *Diagnostic Methods*, 1905 (quotes Luschka), p. 247.

fifth chondrosternal junction. *Mitral*: Behind the left half of the sternum at the level of the fourth costal cartilage.¹¹

Aortic: Behind the midsternum at the level of the third intercostal space. *Pulmonary*: Behind the third left chondrosternal articulation. *Tricuspid*: Behind the lower portion of the sternum at the level of the fourth intercostal space. *Mitral*: Behind the fourth chondrosternal articulation.¹²

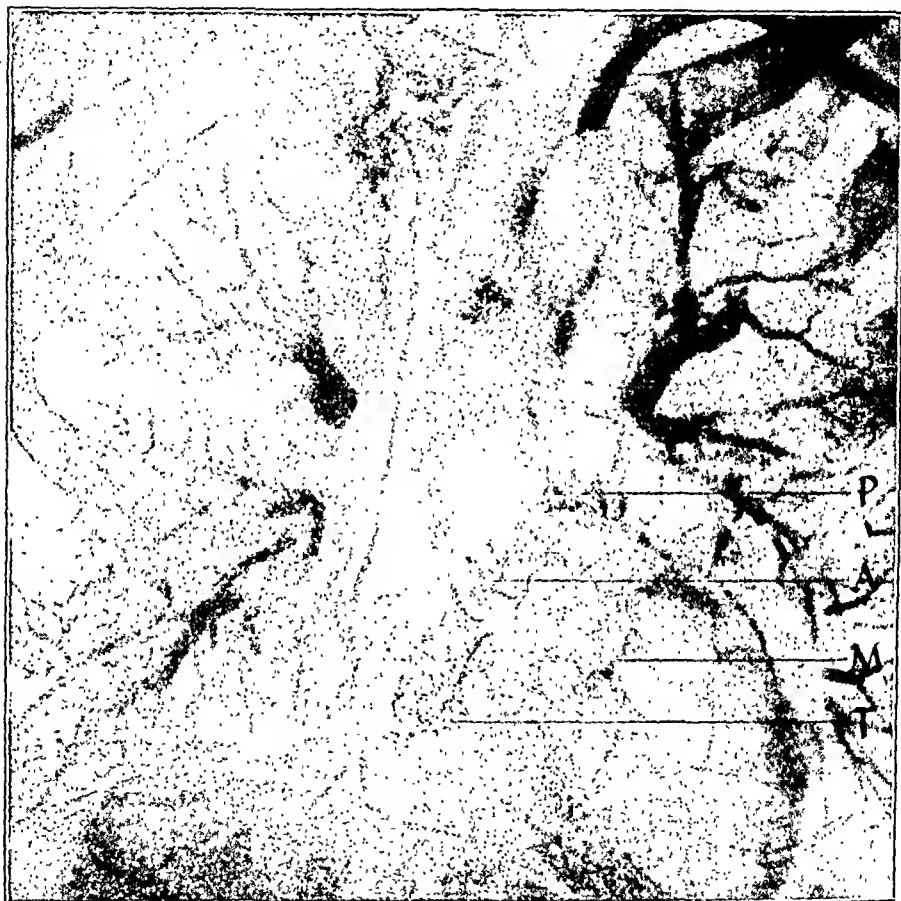


FIG. 5.—X-ray picture of the thorax, a frontal section of which is shown in Fig. 4. The valves in this plate are photographed rather faintly. They are more widely separated than is usually found, the condition being probably due to cardiac dilatation. The aorta, the pulmonary artery, the left auricular appendix (see Fig. 4), the pulmonary veins and the internal mammary and coronary arteries are shown with great clearness. P, pulmonary valve; A, aortic valve; M, mitral valve; T, tricuspid valve.

Aortic: Behind the left half of the sternum, opposite the lower part of the third chondrosternal articulation. *Pulmonary*: Behind the third left chondrosternal articulation. *Tricuspid*: Behind the midsternum, opposite the fourth chondrosternal articulation and

¹¹ J. C. Da Costa, Jr., 1911, p. 298.

¹² Joh. Sobotta, Atlas and Text-book of the Human Anatomy, American Translation, 1906, ii, 172.

the fourth intercostal space. *Mitral*: Behind the left half of the sternum opposite the third interspace and the fourth chondro-sternal articulation.¹³

Aortic: Behind the left half of the sternum a little below and to the right of the pulmonary. *Pulmonary*: Behind the sternal end of the third left costal cartilage. *Tricuspid*: Almost behind



FIG. 6.—Frontal section of the thorax, the x-ray picture of which is shown in Fig. 7.

the midsternum, opposite the fourth interspace and the fifth chondrosternal articulation. *Mitral*: Opposite the sternal end of the third left interspace.¹⁴

Aortic: The third interspace close to the sternum. *Pulmonary*: At the junction of the third rib with the left side of the sternum. *Tricuspid*: Behind the sternum, near the middle line about the

¹³ D. J. Cunningham, *Text-book of Anatomy*, 1906, p. 789.

¹⁴ G. A. Piersol, *Human Anatomy*, 1907, p. 692.

level of the fourth costal cartilage. *Mitral*: Behind the third intercostal space about one inch to the left of the sternum.¹⁵

Aortic: Behind the inner edge of the third costal cartilage, intercostal space, and contiguous portion of the sternum on the left side. *Pulmonary*: A little higher and more to the left. *Tri-cuspid*: Below and a little to the left, a line drawn from the inner

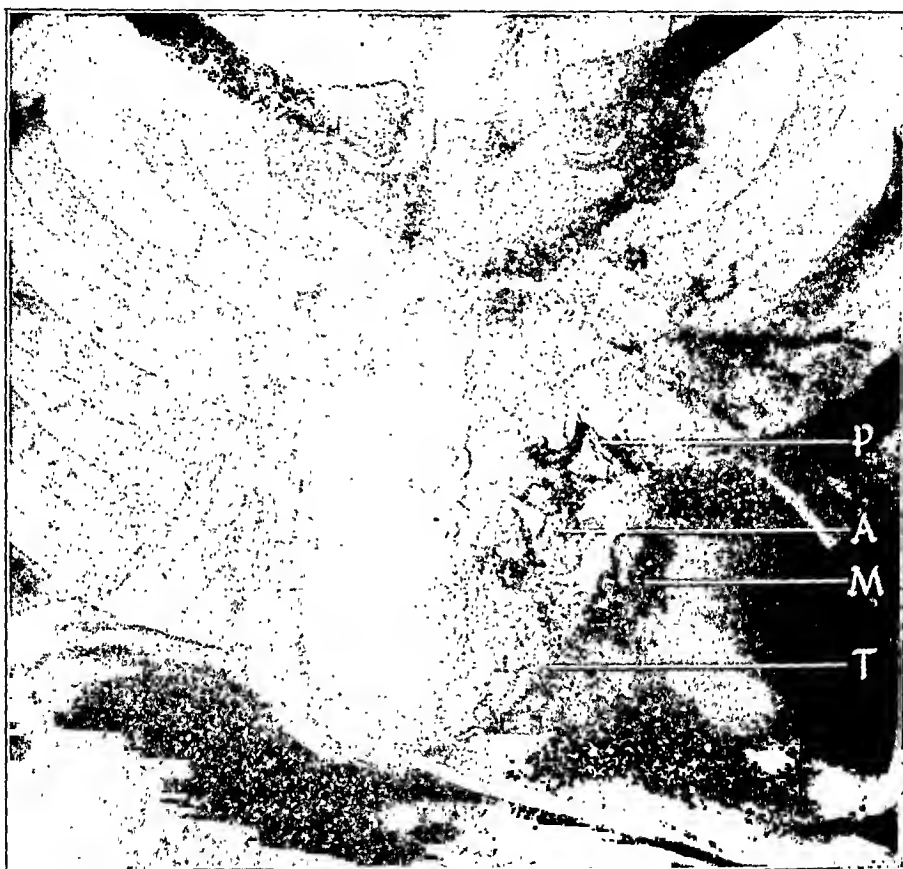


FIG. 7.—X-ray picture of the thorax, a frontal section of which is shown in Fig. 6. The individual leaflets of the pulmonary and aortic valves are shown with unusual distinctness. All the valves lie approximately one rib below what is described as their normal position. *P*, pulmonary valve; *A*, aortic valve; *M*, mitral valve; *T*, tricuspid valve.

end of the third costal cartilage on the left to the inner end of the sixth right costal cartilage. *Mitral*: Behind the third intercostal space about one inch to the left of the sternum.¹⁶

With the view of settling definitely these moot points the present study was undertaken. In the planning of our investigations the problem naturally divided itself into two parts, (1) the preparation of the material so that conditions existing during life would be present for postmortem study, and (2) the depiction of such con-

¹⁵ H. Morris, *Human Anatomy*, Philadelphia, 1895, p. 972.

¹⁶ J. Leidy.

ditions with all possible sources of error eliminated. In order to secure these desiderata the following plan was evolved: Each cadaver on being delivered at the University of Pennsylvania was injected with 10 per cent. formaldehyde solution and then put into cold storage. When thorough freezing had been secured the head and neck, the upper extremities, and the lower part of the trunk were cut off. The thorax was then cut into frontal sections about one inch thick, the cuts being made parallel with the anterior surface of the chest. Each section was then cleaned up by removing all blood clots and saw detritus from the heart cavities and large bloodvessels. In this manner we avoided distortion, since all parts were hardened in the position which they occupied at death.

To depict the conditions present we adopted the following procedure: Each valve leaflet was carefully dried and then painted with the thickest possible lead paint. This was readily done, for the sections were so thin that all the valves were accessible, and in most instances it was possible to paint both surfaces of the entire eleven leaflets.

Finally, after the valves were painted, the sections were superimposed, with the anterior one below, and an x-ray photograph taken. In order to show with greater clearness the relations of the valves to the sternum and ribs, that section of the thorax which comprised the posterior portion and included the vertebral column, the posterior section of the ribs and the thick spinal muscles, was not used. By discarding this portion nothing was lost and much was gained in clarity, since the vertebræ and the posterior part of the ribs were eliminated from the pictures.

In the course of our investigations fifteen bodies were sectioned. It was soon evident, however, that a much larger number would have to be studied before any definite conclusions regarding normal relations could be reached, since many of the cadavers represented pathological alterations in the topography of the thoracic viscera. Often the heart was displaced as the result of extensive pulmonary tuberculosis, or of hypertrophy of the heart. Other lesions, such as pericardial effusions, atelectatic lungs, etc., furnished additional sources of error.

We therefore offer this communication in the nature of a preliminary report, and in demonstration of an entirely feasible and hitherto unemployed method of studying post mortem the topography of the heart valves in health and disease.

In conclusion, we wish to express our indebtedness to Dr. Henry K. Pancoast for his kindness in furnishing us with the x-ray photographs.

THE ROLE OF THE STETHOSCOPE IN PHYSICAL DIAGNOSIS.

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THE object of auscultation is threefold: (1) It should bring to the ear intracorporeal sonorous vibrations; (2) from the nature of the sound we deduce the physical conditions producing it, and (3) finally we attempt to judge the significance of these conditions to the vital economy of the patient.

Mediate auscultation through the stethoscope is so well established that immediate auscultation by direct application of the ear to the body may well-nigh be numbered among the lost arts. Nevertheless, Conner¹ has called attention to the surprising fact that certain pathological sounds, as the diastolic murmur of aortic insufficiency and the amphoric note from the bronchi, may be missed through the stethoscope while plainly audible with the unaided ear. It is well to have such possibilities in mind when the constant refinement in instrumentation, particularly as manifested in the German clinic, is, as it were, making the methods of physical diagnosis more and more artificial. The designer of a stethoscope is happy to make the sounds which it transmits as loud as possible, yet he may be sure that this loudness is but the result of sympathetic vibration of the instrument itself, and it is hardly possible to construct an apparatus which will at once magnify in equal ratio all the tones that come to it. F. von Müller² has recently demonstrated that the normal inspiratory murmur is much lower in pitch than the note obtained from the trachea or bronchi. He used as a stethoscope-resonator a rubber tube whose length could be varied at will. It required a much longer tube to "speak" in response to the murmur of inspiration than to the note from the trachea. It is always to be suspected that any extraordinary intensity of auscultated sound is due to selective resonance on the part of the instrument used. The roar from a bull-frog's pouching chops probably represents inadequately the range of partial tones emitted from his larynx.

It may be admitted, as a general fact, that there is no such thing as a sonorous vibration within the chest, but it comes to the ear modified by the sympathetic resonance and conductive properties of the tissues of the thorax; judgments founded on auscultatory findings represent only the more or less conscious appre-

¹ Certain Limitations of the Stethoscope (Binaural) and Their Clinical Importance, New York Med. Jour., 1907, lxxxvi, 56.

² Zur physikalischen Diagnostik, 1911, xxviii, Kong. f. innere Med., 181.

ciation of the way in which sonorous vibrations are modified by definite physical changes in the tissues.

The simple fact of tactile fremitus is a demonstration of the power with which the wall of the chest may reproduce vibrations originating in the larynx. It has been pointed out by Coplin,³ by the writer,⁴ and by others, that certain pathological sounds have their origin in the chest wall itself, though they imitate the sonorous effects of underlying disturbances. The importance of the chest wall as a resonator for visceral vibrations has appealed to me for many years, and the belief has gradually developed that the experimental modification of mural vibrations during physical examination gives unwonted clarity to the perception of the conditions within the thorax. The procedures applicable to the examination of the heart were published in 1897,⁵ while a consideration of them in the study of the lungs has recently been detailed.⁶

In brief the method purports to enable the examiner to apprehend at will the sonorous vibrations intrinsic to the thoracic viscera unconfused with those proper to the chest wall itself. This result is accomplished by damping the mural vibrations by pressure applied to the chest piece of the stethoscope. The astounding predominance of the mural component of the sounds to which we are accustomed to listen in the chest becomes especially obvious through the auscultation of those normal lungs in which vocalization is accompanied by considerable tactile fremitus—as in vigorous young men.

The powerful, resonant voicing heard through the stethoscope when applied lightly to the chest is usually turned into a flat, feeble, and distant sound when the bell of the instrument is pressed firmly upon the skin. This effect of stethoscopic pressure is much more marked below the level of a plane transecting the body at about the level of the fourth rib in front. As was pointed out in a previous paper,⁷ the vibrations of the air in the trachea and large bronchi penetrate more or less freely directly to the parietes of the upper part of the thorax and are there not annulled by stethoscopic pressure. The sounds heard in the lower parts of the chest are to a much larger proportion made up of sympathetic vibrations of the parietes. This is well demonstrated in the auscultation of the normal inspiratory murmur when it is strongly diffused; pressure usually annuls the murmur over the lower areas, but not above. The normal, breezy inspiratory murmur when not annulled is

³ AMER. JOUR. MED. SCI., 1904, cxxvii, 754.

⁴ Sewall, The Origin of the "New-leather" and "Dry-friction" Sounds Heard on Auscultation, AMER. JOUR. MED. SCI., 1909, cxxxvii, 364.

⁵ Sewall, The Use of Stethoscopic Pressure in Physical Examination of the Heart, New York Med. Jour., 1897, vol. lxi.

⁶ Sewall and Childs, A Comparison of Physical Signs and X-ray Pictures of the Chest in Early Stages of Tuberculosis, Arch. of Int. Med., 1912, x, 45.

⁷ Sewall and Childs, loc. cit.

usually greatly diminished by stethoscopic pressure, and is rendered sharper, more bronchial, and higher in pitch. These facts have led me to the revolutionary opinion that the normal inspiratory murmur owes its pitch, volume, and quality chiefly to sympathetic vibration of the chest wall.

The influence of the main bronchi on the transmission of sound was recently illustrated in the case of a right-sided serous effusion which reached to about the level of the middle of the scapula. Whispered sounds were plainly transmitted throughout the area of dulness, but failed just above it. When the fluid was aspirated so that its level fell to about the angle of the scapula the whispered sounds could no longer be heard over the remaining effusion. In the first case probably vibrations were taken up by the fluid directly from the right bronchus and its main descending branches, while in the second case the fluid had fallen below the great air vessels and therefore failed to pick up their vibrations.

When the voice is auscultated over a serous effusion in the ordinary way it may show no specific change in character, but on applying pressure the pitch is raised and the quality and duration of the sound are altered in a characteristic manner.

Now if we may assume that the fundamental tone of the chest wall remains practically unchanged while extensive pathological disorders develop in the viscera, it follows that any modification of auscultated sounds due to alteration of conductivity or resonance in the viscera must be relatively exaggerated by any procedure which annuls the mural vibrations. Stethoscopic pressure dampens the mural vibrations and presents to the ear the real acoustic changes in the viscera. The student will observe that the invariable effect of pressure applied to the stethoscope is to raise the pitch of the auscultated note, apparently by cutting off its fundamental and lower partial tones. It has been pointed out by von Müller⁸ that the "chest tones" of the voice, which especially invoke the resonance of the thoracic parietes, belong distinctly to the lower part of the register because the fundamental tone of the chest wall is one of slow vibration.

Interesting results are obtained on auscultating, both without and with pressure of the stethoscope, the normal chests of persons with good singing voice. When a high or "head" note is voiced and held, the sound as heard through the stethoscope applied to the upper chest is little changed, though it is apt to be made more intense and brought nearer the ear by pressure. Near the base of the lungs, pressure decreases the intensity of the sound, but in neither case is there a marked change in the pitch or quality of the note. On voicing a low or "chest tone," however, pressure applied to the stethoscope produces extraordinary changes in the

⁸ Diagnostik der Lungenkrankheiten, Zeitsch. f. ärztliche Fortbildung., 1912, ix, Nr. 14.

sound. With pressure the fundamental tone and apparently the lower partials are damped and the pitch and quality of the transmitted tone are altered and its intensity diminished. It must be borne in mind that it is possible for the thoracic viscera to undergo more or less profound pathological changes without essential modification in their acoustic properties. In such exceptional cases the results of stethoscopic pressure would be negative. Also, although modification from the normal of sounds heard with stethoscopic pressure determines visceral changes with unparalleled delicacy, the specific nature of these changes is not thereby determined; we only apprehend that *something* is the matter.

In previous writings on this subject I have indicated that to successfully damp the vibrations of the chest wall through stethoscopic pressure the physical structure of the stethoscope itself is of fundamental importance. Further study has led to the more definite discrimination of the physical principles involved in the application of "stethoscopic pressure," and briefly to set them forth is the object of this paper.

A solid body laid upon the chest wall takes up and transmits according to its own elastic properties the vibrations emanating from the latter. When the pressure of the solid body upon the surface is sufficiently increased the sensible vibrations of the latter are damped, but their energy is, of course, transferred to the body which extinguished them. When, for example, the uniaural, solid stethoscope is applied to the chest the sounds heard through it are not deadened by increasing the pressure of contact; on the contrary, they tend to become more intense, and are brought nearer the ear.

The same result is obtained with the use of the binaural air-conducting stethoscope, in which the ear and chest pieces are connected by a conducting solid medium, such as a spiral wire. With the simplest form of binaural stethoscope, however, in which the ear and chest pieces are joined by plain rubber tubes, the results of pressure are wholly different. If the bell of such a stethoscope is thick-walled and has a high fundamental tone the damped mural vibrations do not sensibly affect it, and therefore there come to the ear only such vibrations as are transmitted from the viscera of the thorax through the disk of tissue enveloped by the stethoscope bell. If the chest-piece of the stethoscope is thin-walled, and therefore easily set into vibration, or, as in certain popular and excellent instruments, is provided with a disk designed to vibrate, the vibrations set up in the chest piece will not be annulled by pressure, but will be transmitted to the air of the rubber tubes and conducted to the ears.

Our conclusions may be condensed as follows: The sounds heard in auscultation of the chest are compounded of both visceral and mural vibrations, of which the latter, especially in the lower

parts of the musical scale, may greatly preponderate in intensity, but of which the former are alone usually of clinical interest.

The *quasi* adventitious sounds due to sympathetic vibration of the chest wall may be damped and rendered more or less inaudible by firm pressure applied to the bell of the stethoscope. In order to thus annul the sound from mural vibrations the instrument must transmit by pure air conduction, and its chest-piece must not itself sensibly take up the vibrations of the chest wall.

A CLINICAL AND EXPERIMENTAL INVESTIGATION OF THE THERAPEUTIC VALUE OF CAMPHOR.

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THE profession has long felt the need of a more accurate knowledge in regard to the relative value of the several drugs employed as so-called "circulatory stimulants." Since this problem first occupied the minds of the writers, important contributions have been made. The present communication appears to be justified, nevertheless, because of the obscurity which still surrounds many members of the group. Thus as concerning the therapeutic value of camphor there has been so far rather more of speculation than of positive knowledge.

A study of some of these drugs was contemplated by us as early as the autumn of 1909. However, the present research was directly stimulated by observation of the following case: In the spring of 1910 a relative of one of us died as the result of a widespread infection, secondary to a suppurative cholecystitis. During the last three weeks of the patient's life there were several periods of alarming circulatory breakdown, occurring during the course of a clinical auricular fibrillation. These acute seizures were apparently due to the action of the infective agents upon the myocardium and vasomotor apparatus. During the attacks, attempts were made to improve the mass movement of blood by the hypodermic administration of such substances as caffeine, strychnine, and camphor. The use of camphor was followed in more than one instance by a marked temporary improvement in the character of the pulse and in the general condition of the patient. Nevertheless, the general course of the disease was downward.

On the last day of the patient's life hypodermic medication by camphor was frequently employed in the hope of influencing favorably a gradually failing circulatory apparatus. This treatment was without apparent effect, except that it resulted in annoyance to the patient, and added distress to his family.

A resort to frequent hypodermic injections in the face of an almost hopeless condition had often been observed by us, but it is evident that, to be justifiable, such interference must be expected to result occasionally in benefit to the patient. Any rational confidence in therapy must necessarily be based upon a knowledge of at least the results which may be expected from the exhibition of a remedial agent. Such knowledge was lacking in regard to camphor, the one remedy which had appeared to benefit the above-mentioned patient. Therefore, we decided that our proposed investigation of the cardiac stimulants should be inaugurated by a study of this drug.

The method of bedside study which was subsequently followed by us owed its inspiration to Dr. James MacKenzie, whose brilliant work upon members of the digitalis group has had such a far-reaching effect in stimulating the clinical study of drugs in their action upon the human circulatory apparatus. In addition, coincident laboratory experiments were instituted, the object of which was the determination of the effects of camphor upon the lower animals.

We had for some time shared the belief that the best hope for advance in practical therapeutics lay in the close coöperation of clinical and laboratory workers. To this end, therefore, our bedside and laboratory results on camphor have been frequently compared, and mutually criticised during the course of the ensuing experiments. When the investigation was already well under way the Council of Pharmacy and Chemistry of the American Medical Association formulated its admirable plan of coöperative clinical study of the cardiac stimulants. The proposed method of clinical investigation as recommended by it closely corresponds with that which had been independently adopted by one of us, and which was then being followed in our work with camphor.

The present communication is of a preliminary character, and represents the results obtained thus far in our combined research.

In reading the available literature on camphor one is impressed by the great diversity of opinion as to the mode of action, toxicology, and therapeutic value of the drug. Moreover, reports as to the clinical utility of camphor, although often enthusiastic, are apt to be unconvincing. There is, nevertheless, a widespread belief in camphor as an efficient "heart stimulant." In response to inquiry one may learn that many competent practitioners still rely upon the drug as the best which can be employed in combating a sudden failure in cardiac force, or impairment in vasomotor tone, or both. Moreover, one may find that the hypodermic use of

camphor in oil is frequently resorted to in ambulance work, in the operating room, and at the bedside, in order that an apparently impending circulatory failure may be averted.

Extremely divergent views are held as to the dosage of camphor. Thus, it appears that the customary hypodermic dose in America and England is about 3 grains, whereas in Germany the average dose is much larger. The following references are illustrative.

Hirschfelder¹ says that the average dose of camphor in oil is 2 grains.

Sollman² gives the dose as 1 to 5 grains and Cushney³ as 2 to 10 grains.

Allbutt⁴ writes: "Of the larger doses of camphor used by some physicians in heart failure I have no personal experience, and I should be a little timorous of giving it in doses of from 5 to 20 grains as recommended by some authors. Nevertheless, the drug is well spoken of as a cardiac restorative, and much of this testimony is by physicians whose opinion is not to be overlooked."

The issue of the *Therapeutic Gazette* for June 15, 1912,⁵ contained an editorial article commenting on the use of camphor. Webster's article⁶ was quoted in which that author advocated the employment of the drug in pneumonia in a daily dose of 30 grains. This dose was regarded by the editorial writer as excessive and dangerous, and he stated that he believed that "If 1 or 2 grains fails to do good, then larger doses will not produce beneficial results."

An abstract in the same journal⁷ cites several cases of alleged poisoning by this drug; the author, however, admits that poisoning by camphor is rare and generally not fatal. In several instances he admits that the quantity ingested was exceedingly small. Thus one case of fatal poisoning is said to have occurred as the result of eating candy containing camphor, while Blyth is quoted as of the opinion that from 7 to 40 drops of Rubin's spirit of camphor have produced coma, convulsions, and partial paralysis.

Hausemann⁸ has collected 30 cases of camphor poisoning principally from the field of the older English literature. He mentions instances in which a few drops of spirit of camphor had caused severe collapse, convulsions, and coma. Further references are made to "self-experiments," in which the ingestion of 2.5 grams of camphor have resulted in cramps and convulsions.

Kobert⁹ gives the therapeutic dose as 0.1 to 0.2 gram in oil.

¹ Diseases of the Heart and Aorta, 1910, p. 183.

² Text-book of Pharmacology, 1903, p. 465.

³ Pharmacology and Therapeutics, 1910, p. 73.

⁴ Practical Treatment, edited by Musser and Kelly, 1911, ii, 55.

⁵ The Use of Camphor as a Diffusible Stimulant, xxxv, 406.

⁶ Medical Record, lxxix, 145.

⁷ Therapeutic Gazette, May 15, 1912, p. 344.

⁸ Handb. der ges. Arzneimittellahre, ii, 964, Berlin, 1875; Hausemann und Hilgen, Die Pflanzenstoffe, 2 Aufl., i, 555.

⁹ Lehrbuch der Pharmakotherapie (43), 45 Stuttgart, 1897.

The following references support the view that camphor may be used with safety in larger doses than those above mentioned: v. Leube cited by v. Jakseh,¹⁰ gave 20 grams in a day to a patient with heart failure.

Vogl¹¹ recommends as many as 4 grams as a dose.

Happich¹² states that from 5 to 15 grams of camphor or from 25 to 75 c.e. of 20 per cent. camphor in oil may be injected subcutaneously in a day.

Sehmiedeberg,¹³ on the other hand, writes that a man will be surely severely poisoned by taking a dose of 10 to 15 grams, but that a medium-sized dog can eat 30 grams in a day without dangerous symptoms. This author calls attention to the fact that members of the canine family are not affected by the smell of camphor; yet this odor is obnoxious to the cat.

Happich¹⁴ states that the lethal dose by the mouth for the dog varies greatly. From 8 to 20 grams were given without bad results, and one dog received 20 grams a day during a period of ten days without poisoning.

Seibert¹⁵ reports the use of 2.4 grams of camphor in oil injected subcutaneously every twelve hours in the treatment of pneumonia, and states that even 10 c.e. of 30 per cent. camphor in oil causes no poisoning when injected hypodermically every eight to twelve hours.

Webster, during a period of four days, has employed camphor hypodermically in daily doses of 30 grains without the production of untoward symptoms.

Schlutz¹⁶ found that in infants weighing 2400 to 4500 grams, 0.15 to 0.3 gram of camphor could be given by the mouth without the production of dangerous symptoms, but that in cases of malnutrition a relatively smaller dose could cause intoxication.

The above examples suffice to indicate the extreme divergence of opinion among authors as to the safe doses of camphor. While some fear to give more than 2 to 5 grains, others claim that ten times this amount may be administered without bad effect. The explanation of the variation in the results obtained from the administration of camphor may be found in part in the metabolism and excretion of the drug.

Schmiedeberg and Meyer¹⁷ found, as Wiedemann before them had found, that when camphor is absorbed it quickly unites with glycuronic acid and is rendered inert. It is subsequently excreted in the urine as camphoglycuronic acid. However, a

¹⁰ Nothnagel's Spec. Pathologie, 1897, S. 380.

¹¹ Eulenberg's Realenzyklopadie, Kampfer.

¹² Mittheilungen aus den Hamburgischen Staats-Krankenanstalten, 1908, (8) 1.

¹³ Pharmakologie, 1909, S. 274.

¹⁴ Loc. cit.

¹⁵ Medical Record, 1912, p. 743.

¹⁶ Zeitsch. f. Kinderheilkunde, 1911 (1), 197.

¹⁷ Zeitsch. f. physiolog. Chemie, 1907 (3).

variable fragment may escape such combination and be excreted uncombined by the lungs. It is this fragment which is regarded as responsible for the physiologic action of the drug.

Happich found that camphor caused death in emaciated or CO₂ asphyxiated rabbits, whereas glycuronic acid with camphor injected intravenously into such animals caused no intoxication. This authority also remarked that this finding explains why one dog may be killed with 8.5 grams of camphor while another may receive even 20 to 25 grams without injury.

Schlutz¹⁸ believes that in this fact lies the explanation of the toxic symptoms produced by camphor in the poorly nourished infants studied by him. He thinks that in such cases there is probably not enough available glycuronic acid to unite with the camphor, and that the uncombined fragment is accordingly greatly increased in amount. Therefore, intoxication results; whereas, in well-nourished infants there is enough glycuronic acid to unite with nearly all of the camphor, and hence the unchanged fragment is so small that no intoxication occurs even after relatively large doses.

If the foregoing supposition be correct it becomes evident that care should be exercised in the administration of camphor to those patients who have a poor glycuronic acid content. This condition may be suspected in cachexia, in starvation, and in cases of CO₂ poisoning, of severe sepsis, of eclampsia, etc.

It is not the purpose of this communication to deal with the toxicology and action of camphor upon the tissues and organs not directly associated with the circulatory organs. It may, however, be observed that there is good evidence that camphor may act as an excitant on the central nervous system and as an irritant to the gastro-intestinal tract. Small doses, according to Schmiedeberg, induce cerebral symptoms such as dizziness, headache, confusion of ideas, and delirium. With large doses (10 to 15 grams) severe poisoning occurs, evidencing itself by pain in the stomach, hallucinations, and convulsions. However, these symptoms later subside and complete recovery follows.

The evidence in regard to the effect of camphor upon the cardiovascular system is of a contradictory character. The drug is said to cause a periodic increase in blood pressure in the curarized animal, an effect due to its action on the vasomotor centre. On the heart, small doses cause an increase in rate and force of beat, due to stimulation of nerve endings and of heart muscle. In larger doses there is a concomitant weakening of heart action. Experimentation upon the dog shows that the intravenous injection of 0.04 to 0.1 gram causes a lowering of blood pressure. (Schmiedeberg.)

On the other hand the work of Roth¹⁹ shows that camphoric

¹⁸ Loc. cit.

¹⁹ Jour. Pharm. and Exper. Therap., 1911, ii, 405.

acid is practically without effect upon the circulation. This author found that early in the experiment there was a small sustained rise in blood pressure following either a large or a small dose, but he observed that later the same dose caused a sustained fall. The heart rate was decreased in all but one instance. Roth attributes these results to salt action, and does not consider camphoric acid itself as a heart stimulant.

Cushney believes that the only result obtainable from therapeutic doses of camphor is a slight dilatation of bloodvessels, a condition due to peripheral action. Sassen²⁰ claims that after small doses (0.1 to 0.5 gram) the pulse becomes fuller and stronger, while after large doses (0.8 to 2.0 gram) its frequency and fulness are diminished.

It appears to be fairly well established that camphor can restore the heart after poisoning with chloral, muscarine, strychnine, and such other drugs as are thought to depress the irritability of the cardiac muscle.

Böhme²¹ found that camphor restored the heart after chloral poisoning.

Harnack and Witowski²² found that muscarine standstill of the heart is removed by camphor.

V. E. Henderson²³ agrees with Böhme. He found that an interference with rhythm brought on by chloral could be frustrated by camphor.

Maki²⁴ observed that the low blood pressure caused by chloral poisoning was greatly raised (38 to 80 mm.) by camphor.

Laangard and Maass,²⁵ using a preparation of dextro, levo, and inactive camphor were not able to demonstrate any action on the normal frog's heart after poisoning the heart with camphor. Hämäläinen²⁶ found that camphor can restore the frog's heart after it has been damaged by chloral according to Bohme's²⁷ method.

Thus it is evident that the results of laboratory investigation strongly support the view that camphor is antagonistic to the depressing effect upon the heart of chloral, and also of muscarine and strychnine.

There is also some laboratory evidence that camphor may restore coördinate contraction of the heart which has passed into fibrillation.

²⁰ Vergleichende Untersuchungen über die Wirkung einiger Kampferarten, Inaugural Dissertation, 1909.

²¹ Archiv f. exp. Path. u. Pharm., 1905, lii, 346.

²² Arch. f. exp. Path. u. Pharm., 1876, v, 401.

²³ Jour. Pharm. and Exper. Therap., 1911, ii, 153.

²⁴ Ueber d. Einfl. des Camfers, Caffeines, und Alkaloids auf das Herz, Inaugural Dissertation, Strassburg, 1884.

²⁵ Therap. Monats., 1907, xxi, 513.

²⁶ Skand, Arch. f. Physiol., 1908, xxi, 64.

²⁷ Loc. cit.

Seligman²³ found that fibrillation of the cat's heart was promptly relieved by camphor, and also discovered that he could not establish lasting fibrillation of the heart while it was being perfused with camphor. Fibrillation occurred only during the application of electrodes, upon the removal of which the fibrillation ceased.

Kronecker²⁹ called attention to the difference which he believed to exist between the heart of the cat and that of the dog. He stated that he had studied over two hundred fibrillating hearts of the dog without ever having witnessed a recovery from fibrillation, while in the cat heart, spontaneous recovery from fibrillation is not unusual.

Gley,³⁰ on the other hand, has found that the heart of a newborn puppy is highly resistant to faradization, so that under ordinary conditions, after the removal of the electrodes, normal rhythmic contractions are resumed.

In planning our bedside study of camphor, we decided to limit the investigation to the effects of the drug, as administered hypodermically, upon the circulatory apparatus of human subjects exhibiting varying conditions of the cardiovascular apparatus. We believe that a clinical study of the effect of a drug upon the circulatory system should include observations on the following conditions: changes in the force, frequency, and rhythm of the heart beat; variations in peripheral resistance; alterations in the volume of the blood. Definite results, if obtained, should be analyzed by eliminating vagus action by atropine, by the study of polygraphic tracings, and by a comparison with results obtained in the laboratory.

For the purpose of the present investigation, camphor was dissolved in oil and administered subcutaneously. The drug was obtained from several sources of supply, and was either dissolved under our direction, or obtained in ampullæ specially prepared for hypodermic use. The administration was by single or multiple subcutaneous or intramuscular injection into patients who could be somewhat arbitrarily divided into the following groups:

- A. Patients whose circulatory apparatus was apparently normal.
- B. Those whose auricles were in clinical fibrillation (confirmed by polygraphic tracings).
- C. One patient (2 observations) with valvular disease but normal rhythm.
- D. Patients with unclassified cardiovascular diseases, chiefly, however, affecting the myocardium and vascular coats.

In addition to the above, two control experiments were conducted. Sterile oil was injected into a patient of Group A and into one of Group B. All the subjects but one were adults in a state

²³ Archiv f. exp. Path. u. Pharm., 1905, lii, 333.

²⁹ Zeitschr. f. Biologie, 1896, xvi, 529.

³⁰ Archiv. de Physiologie, 1891, iii, 735; Soc. de Biologie, 1891, 108.

of nutrition from fair to good. Records of pulse and of systolic and diastolic blood pressure were made at frequent intervals covering a period of forty to two hundred and seventy minutes after the injection of the drug; the usual duration of the observation was about one hundred and twenty minutes. The patients were frequently questioned as to the presence of subjective symptoms which might be attributable to the camphor, but in not a single instance was there obtained any evidence of drug action, with the exception of a complaint of burning at the point of administration. The latter sensation was frequently accompanied by local redness and swelling, which lasted for several hours.

This study was carried on under such circumstances as made an estimation of the volume of the blood impracticable. Polygraphic tracings were taken in several of the fibrillation cases before, during, and after the use of camphor, but in no instance was there observed any alteration in the type of radial or venous pulse as the result of the medication. Blood pressure was estimated by the auscultatory method, a Stanton and a standardized Tycos instrument being employed. The point of disappearance of the second sound was recorded as an admittedly unsatisfactory indication of diastolic pressure. During certain of the experiments it was unfortunately impossible to repress the action of such extraneous influences as mental excitement and muscular action. The atropine test did not appear to be indicated in any experiment. Reference to the table which follows will show the type of subject and dosage employed in each experiment, together with the character of pulse as to rate and rhythm, and the systolic and diastolic blood pressure as recorded before and after the administration of the camphor.

The table given below may be summarized as follows:

1. Controls: Injection of sterile oil containing no camphor. (Class A and B.) A single observation was made upon each of two patients. The following variations were noted during the time of observation: systolic pressure, 13 mm.; diastolic pressure, 10 mm.; pulse rate, 12 beats.

2. Patients with apparently normal circulation: (Class A) five observations. In only one (Experiment 5) was there any distinct change in the circulation. The patient showed, seven minutes after the hypodermic injection of 20 grains of camphor in oil, a fall of about 17 mm. in systolic pressure and 25 mm. in diastolic pressure.

3. Patients with auricular fibrillation and various cardiovascular lesions: (Class B) nine observations. In only three was there any distinct change. In Experiments 2 and 3, one observation each, there was a distinct rise in diastolic pressure, and a slight rise in systolic pressure ten minutes after the administration of camphor. One patient received ten grains and the other twenty grains.

Date.	No.	Condition of patient before administration.					Administration.		Condition after administration.				Summary.	
		Sex.	Age.	Weight in kilos.	Group.	Pulse.	Diastolic pressure.	Systolic pressure.	Dose.	Time elapsed, minutes.	Pulse.	Diastolic pressure.		Systolic pressure.
						Rhythm.	Rate.							
Oct. 2, 1911	1	M.	16	40.0	D.	Regular	84	70 105	Gr. iv Gr. viij, 150 minutes later	30 30	Regular Regular	82 90 105 92 68 112		S. P., rise of 7 and 10 mm. in 15 and 20 minutes respectively after injection. D. P., rise of 20 and 15 mm. in 30 and 10 minutes respectively after injection. Pulse, initial fall of 8 in first 15 minutes; then progressively increased throughout experiment.
Oct. 4, 1911	2	M.	Circa 30	66.8	B.	Very irregular	72	70 130	Gr. x	10	Very irregular	84 110 120		Rise in S. P., D. P., and Pulse in first 10 minutes. All reached starting level at end of experiment (40 minutes).
Oct. 6, 1911	3 Same patient as No. 2	M.	Circa 30	66.8	B.	Grossly irregular	65	90 132	Gr. xx	10	Grossly irregular	70 125 150		S. P., sustained rise of 8 to 18 mm. throughout experiment. D. P., initial rise of 35 mm.; sustained average of 25 mm. Pulse, rise of 15 beats 40 minutes after injection; 20 starting level in 1 hour.
Oct. 10, 1911	4	M.	45	?	Broken compensation C.	Regular	90	99 130	Gr. xx	20	Regular	92 120 132		S. P., negative. D. P., rise of 21 mm.; not sustained. Pulse, rise of 14 to 22, 30 and 60 minutes respectively after injection.
Oct. 12, 1911	5	M.	37	80.0	A.	Regular	68	115 132	Gr. xx	10	Regular	68 90 122		S. P., initial fall of 17 mm.; sustained fall of 7 to 17 mm. for 1 hour. D. P., initial fall of 25 mm.; sustained fall of 10 to 20 mm. for 1 hour. Pulse negative.
Oct. 23, 1911	6 Same patient as No. 4	M.	45	?	Compensation nearly restored C.	Regular	80	80 95	Gr. x, 25 minutes later	10 15	Regular Regular	78 80 97 70 77 97		S. P., negative. D. P., negative. Pulse, negative. Compare results C, No. 4.
Nov. 2, 1911	7	M.	70	90.0	B.	Marked arrhythmia	74	215	Gr. xij	55	Marked arrhythmia	70 .. 260		S. P., during 55 minutes rise of 45 mm. Marked psychic agitation during experiment. Pulse, unaffected.

Date.	No.	Condition of patient before administration.					Administration.		Condition after administration.				Summary.	
		Sex.	Age.	Weight in kilos.	Group.	Pulse.		Dose.	Time elapsed, minutes.	Pulse.		Diastolic pressure.		Systolic pressure.
						Rhythm.	Rate			Rhythm.	Rate			
Nov. 2, 1911	8	F.	70	50.0	B.	Grossly irregular	66	Grs. iij	15	Very ir- regular	68	150	220	S. P., fell 10 mm. during experi- ment. D. P., rise after first and second injection; fall after third. Pulse, probably unaffected.
Nov. 7, 1911	9	F.	36	48.0	Aortic stenosis and insuf- ficiency B.	Marked arrhyth- mia	66	Gr. v later after second dose.	20	Very ir- regular	72	105	122	Negative.
Nov. 15, 1911	10	F.	64	68.0	A.	Regular	78	Gr. xv Gr. x, 55 minutes later	40 30	Regular Regular	72 68	105 115	130 133	S. P., fell 14 mm. after first injec- tion; after second injection no effect. D. P., progressive rise of 17 mm. first hour after second injection. Rise, 5 mm. Pulse, gradually slowed 1 beat.
Dec. 14, 1911	11	M.	42	73.0	A.	Regular	92	Gr. xv Gr. x, 45 minutes later	30 15	Regular Regular	90 92	92 94	117 122	S. P., fall of 13 mm. after first injection; second injection, no effect. D. P., unaffected.
Dec. 2, 1911	12	F.	25	50.0	D.	Regular	64	Gr. xx Gr. x, 45 minutes later	25 15	Regular Regular	76 72	70 76	102 98	Pulse, unaffected. S. P., negative; D. P., negative. Pulse, unaffected.
Dec. 23, 1911	13	M.	20	70.45	A.	Regular	72	Gr. xx	50	Regular	74	84	117	Results negative.
Jan. 2, 1912	14	M.	34	54.0	D.	Regular	90	Gr. xx Gr. x, 40 minutes later	25 30	Regular Regular	84 78	80 85	125 125	S. P., first injection, fall of 15 mm.; second injection, no effect. D. P., negative after both injections. Pulse, gradual fall of 16 beats throughout experiment.
Jan. 6, 1912	15	M.	38	60.0	A.	Regular	55	Gr. xx Gr. x, 65 minutes later	45 30	Regular Regular	62 54	60 75	112 112	S. P., no effect. D. P., no effect. Results negative during 40 minutes previous to adminis- tration of drug. S. P. rose 7 mm. and D. P. rose 10 mm. Pulse rose 5, 10 minutes after first injection; dropped 5, 10 minutes after second injection.

Date.	No.	Condition of patient before administration.					Administration.	Condition after administration.				Summary.
		Sex.	Age.	Weight in kilograms.	Group.	Pulse.	Dose.	Time elapsed, minutes.	Rhythm.	Pulse.	Rate.	
Jan. 24, 1912	16	M.	58	52.0	D.	Regular	Gr. v later Gr. xv, 10 minutes later	25 15	Regular	Regular	70 68	Results negative, including respiration. early F.
Jan. 30, 1912	17	F.	37	55.0	Decompensation B.	Grossly irregular	Gr. xx later	40	Grossly irregular	Grossly irregular	80	S. P., rise of 37 mm. (?) during experiment. 130 Persistent pressure over 130 suggests error in first reading. This patient developed auricular fibrillation while in hospital.
Apr. 1, 1912	18	F.	70	48.0	Marked decompensation B.	Very irregular	Gr. ix later Gr. vi, 55 minutes later	30 20	Very irregular	Regular	120 120	S. P., fall of 10 mm. before injection. Rise of 10 mm. and fall of 5 mm. after injection. D. P., rise after first injection and fall to starting level after second injection. Pulse not affected.
Apr. 19, 1912	19	M.	70	90.0	Marked decompensation B.	Very irregular	6 c.c. sterile oil	15	Very irregular	Very irregular	80	Control experiment; S. P., preliminary rise of 7 mm. D. P., no fluctuations. Pulse same as after camphor; see next experiment.
Apr. 19, 1912	20	M.	70	90.0	Marked decompensation B.	Very irregular	Gr. ix	30	Very irregular	Very irregular	82	S. P., rise but 3 mm. higher than after plain oil. D. P. and Pulse unchanged. Test for glyceruronic acid negative in subsequent 24 hours' specimen of urine.
Apr. 30, 1912	21	M.	36	67.0	A.	Regular	10 c.c. sterile oil 7 c.c. sterile oil, 40 minutes later	30 30	Regular	Regular	68 60	S. P., variation of 13 mm. during experiment. D. P., variation of 10 mm. during experiment. Pulse, variation of 12 beats during experiment.
Apr. 30, 1912	22	M.	67	76.8	B.	Grossly irregular	Gr. xxx later Gr. xx, 40 minutes later	30 30	Grossly irregular	Grossly irregular	96 104	S. P., variation of 8 mm. 50 gr. camphor. D. P., variation of 5 mm. Pulse, variation of 8 beats. Contrast C., Experiment 21.

In Experiment No. 7 there was a rise in systolic pressure of 45 mm. during the first fifty-five minutes following the injections of the drug. The patient was a senile dement and became much excited by the proceedings incident to the experiment. A second observation upon the same patient (Experiment No. 20), under apparently like conditions of decompensation, but with less mental agitation and with a slightly smaller dose of camphor, was negative as to result. In Experiment No. 17, in which the injection of camphor was followed by no result, a subsequent use of strophanthin intravenously during a period of acute dilatation exercised a pronounced effect in slowing the rate and improving the condition of the circulation. In no instance was there any effect upon the fibrillation.

4. Patient with valvular lesions and normal rhythm (Class C). Two observations were made upon one patient. In one observation (Experiment No. 4) there were two sharp accelerations of pulse rate, with a quick return to normal, together with an initial rise in the diastolic pressure which was not sustained. No other changes occurred. Experiment No. 6 was negative.

5. Patients with unclassified affections chiefly myocardial. (Class D): Four patients were considered, with conditions of the cardiovascular apparatus not included in Groups B and C. One observation was made in each of four patients. In two of these experiments, Nos. 1 and 14, more or less fluctuation within narrow limits of both blood pressure and pulse rate was found, but in each instance there was a quick return of blood pressure to the normal. The pulse rate in No. 1 rose fourteen beats, while that in No. 14 fell sixteen beats during the respective experiments.

The laboratory investigations consisted in (1) manometric blood pressure observations upon the unanesthetized animal, using the T-cannula method devised by one of us.³¹ Normal animals were taken as subjects, except in one instance where camphor was administered in large doses to a moribund animal. (2) Perfusion experiments were made upon the isolated heart of the cat.

The laboratory results were in agreement with the clinical findings. Doses of sufficient size to produce slight muscular twitchings failed to cause any distinct rise in blood pressure, or any increase in rate or amplitude of the heart beat in the normal dog. In the moribund dog (one experiment) there was slight transitory heightening of blood pressure together with increased amplitude and rate of heart beat, coincident with mild convulsive seizures, which possibly contributed to the circulatory changes.

The perfusion of the isolated heart of the cat with a saturated solution of camphor in defibrinated blood and 0.9 per cent. sodium

³¹ Heart, 1910, ii, 5.

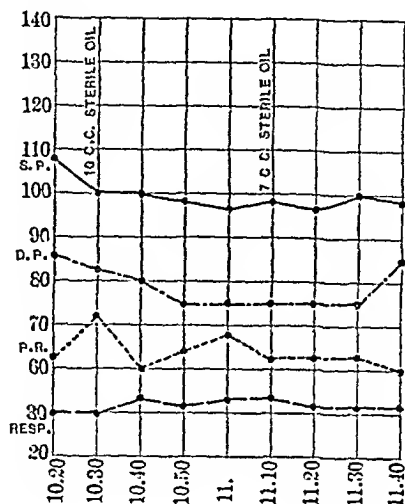


CHART 1.—Observation No. 21. Patient with apparently normal cardiovascular system "control."

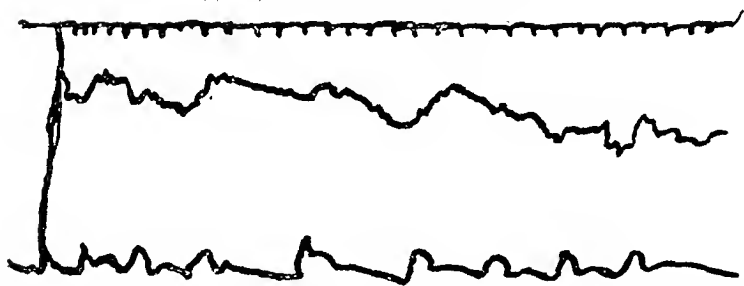
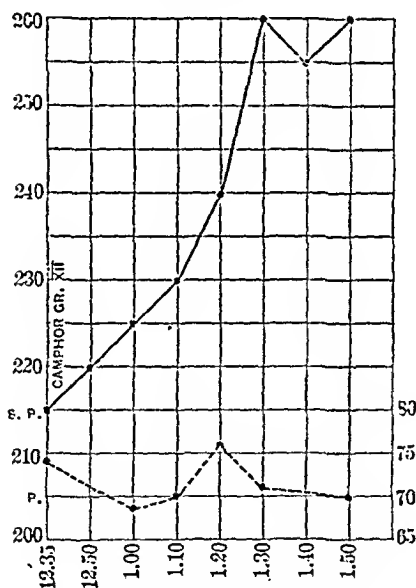


CHART 2.—Observation No. 7. Patient with cardiovascular renal disease; auricle in fibrillation. Many ventricular systoles fail to reach radials. Marked decompensation. Senile dementia. During progress of experiment the patient was greatly excited. There was much voluntary muscular movement, which could not be controlled by the observer. Satisfactory venous tracings were not secured from this patient, as it was impossible to induce him to suspend breathing, while, further, the head was kept in almost constant motion during the attempt.

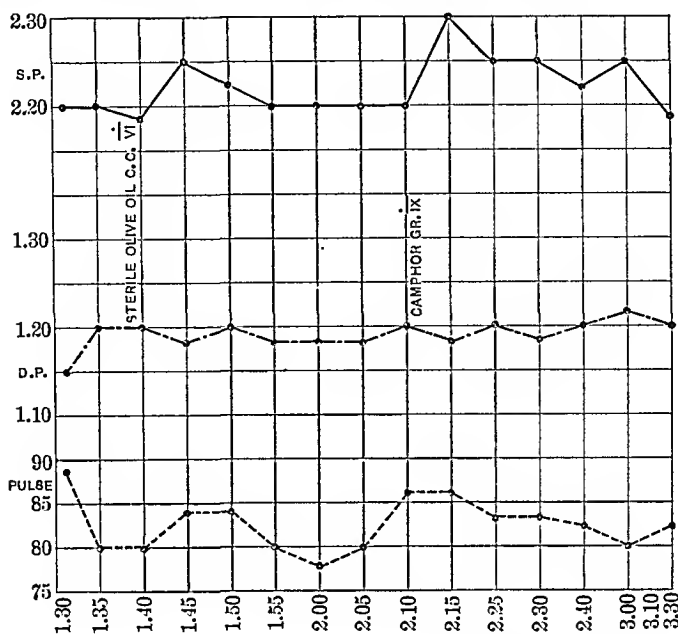


CHART 3.—Observation Nos. 19 and 20. Same patient as in observation No. 7. Condition of patient unchanged as regards fibrillation and decompensation, but as patient was now familiar with the proceeding, there was less mental excitement and muscular movement than was present during the progress of the former experiment.

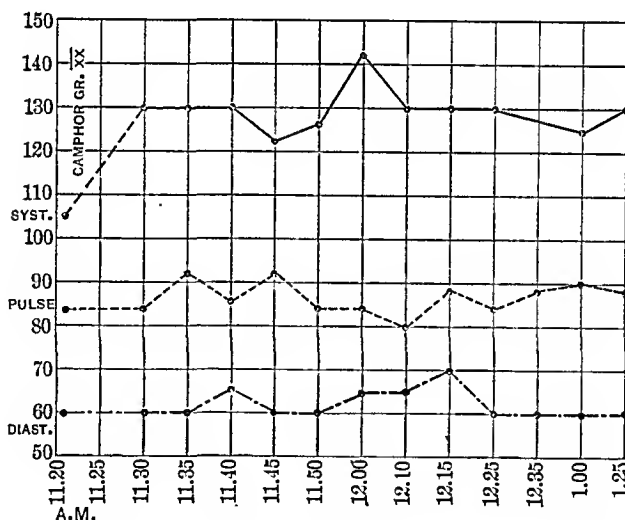


CHART 4.—Observation No. 17. Patient with auricular fibrillation, mitral stenosis, and dilated heart. Patient under the influence of digitalis. Compensation.

chloride solution was without effect upon the normal strongly beating heart. In two instances the fibrillating heart was restored to normal coördinate contractions by perfusion with camphor. The camphor solution employed was, however, a saturated one, and therefore these positive laboratory results should not be interpreted as being in conflict with our negative clinical findings in auricular fibrillation.

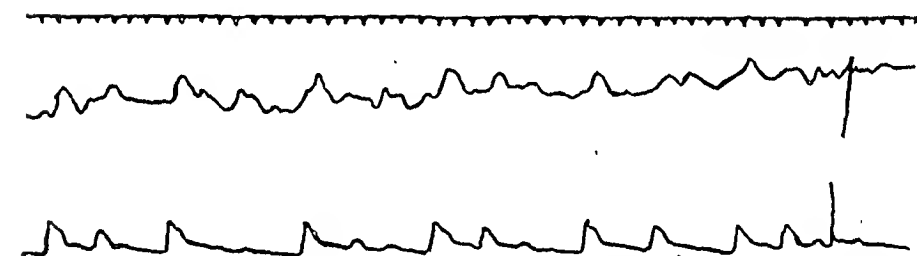
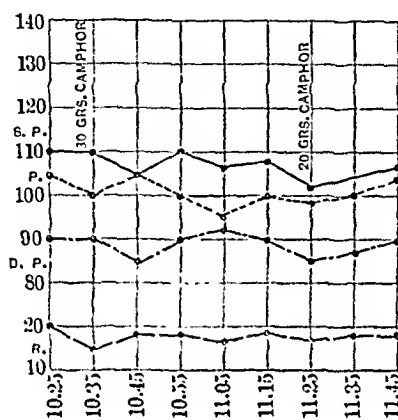


CHART 5.—Observation No. 22. Patient with auricular fibrillation. Compensation. Digitalis.

SUMMARY. In the clinical experiments, camphor injected subcutaneously in oil in doses as large as 50 grains failed to produce any definite effects. The variations in pulse and in blood pressure occasionally following the use of the drug were so inconstant as to make it probable that they had no relation to the medication employed.

The failure of the drug to influence clinical fibrillation of the auricle in the human subject is only in apparent contradiction with our own and other laboratory observations, that perfusion of the isolated cat's heart with camphor may remove fibrillation and restore coördinate contractions. The explanation of this apparent discrepancy is probably to be found in the fact that the dose was greater in the perfusion experiments than was possible in the clinical observations, and that in the former, the condition of fibrillation in the normal heart was induced artificially. A further point to be considered is that different animal species and

varying ages even of the same species show marked differences with respect to fibrillation.

In the single laboratory experiment in which a stimulating effect upon the circulation was observed, the positive result was possibly due to the fact that the animal was emaciated and moribund, and that therefore it may not have been possessed of sufficient glycuronic acid to combine with the camphor.

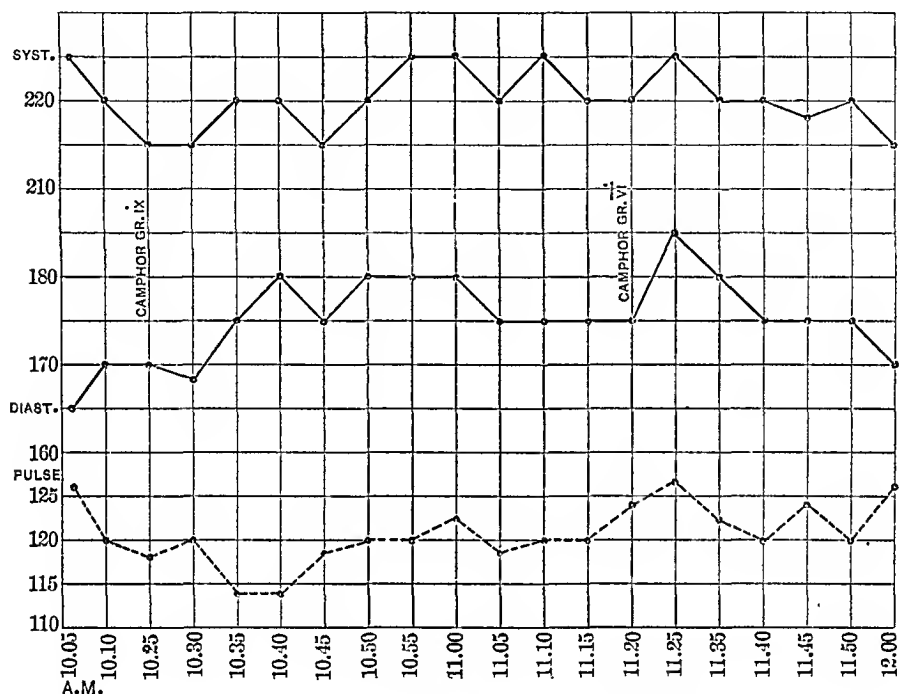


CHART 6.—Observation No. 18. Patient with auricular fibrillation. Marked decompensation. Not under the influence of digitalis.

Therefore, while camphor may be an active agent in certain disorders in which there is an abnormally small glycuronic acid content, and while experiments indicate that the drug exercises a favorable effect upon the heart muscle which is poisoned by chloral, muscarine, or strychnine, nevertheless camphor should neither be relied upon as a cardiac stimulant nor feared as a toxic agent in the doses employed by us and under the conditions studied.

SOME INTERESTING RESULTS WITH THE PHENOLSULPHONE-PHTHALEIN TEST.

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IN the last few years much interest has been directed by the work of Rowntree and Geraghty¹ to the phenolsulphonephthalein test as a means of determining the functional efficiency of the kidneys. As a rule, both in clinical and experimental work,² a close correlation has been found between the impairment in the elimination of the dye and the degree of nephritis, as indicated by clinical symptoms, other laboratory tests, or autopsy findings. Rowntree and Geraghty, however, state that in the study of 25 cases of chronic parenchymatous nephritis they found 5 mild cases of short duration, with only slight edema, which showed a normal excretion of the dye. In cases of longer standing, or cases in which the disease was of ordinary severity, the time of appearance of the drug was always delayed, and the amount excreted was definitely below normal.

The following report of a boy, aged nineteen years, who was admitted to the medical wards of the University Hospital in May, 1912, is of interest because of unusually good phthalein elimination in spite of the existence of a parenchymatous nephritis, with marked epithelial degeneration, and of definite impairment in one of the renal functions, that of chloride elimination. The chief proof of the existence of an anatomical nephritis in this patient is found in the urinary examinations. The urine in twenty-five examinations over a period of three months during which the boy was under observation never failed to show a large amount of albumin, which, estimated by the Esbach method, varied from 2.7 to 8 grams per liter; at the same time an exceedingly large number of hyaline, granular, fatty and epithelial casts, free-fat droplets, and much renal epithelium containing fat droplets were constantly found in the urinary sediment. Ureteral catheterization on July 15, recovered urine with these characteristics from

¹ The Phthalein Test, *Arch. Int. Med.*, 1912, ix, 284.

² J. H. Austin and A. B. Eisenbrey, Experimental Acute Nephritis: The Elimination of Nitrogen and Chlorides Compared with that of Phenolsulphonephthalein, *Jour. Exper. Med.*, 1911, xiv, 366.

each ureter, thus excluding a unilateral lesion. Such a series of urinary findings can scarcely be explained on any basis other than that of a parenchymatous degeneration of the renal epithelium. Additional evidence of nephritis was the presence of a moderate edema of twelve weeks' duration, and, as will be shown later, a slight impairment in chloride tolerance. The etiology of the nephritis has not been discovered.

The complete physical examination revealed slight edema and cyanosis of the extremities, moderate enlargement of the liver, the heart slightly enlarged to the right, and typical auscultatory findings of a moderate mitral stenosis. Within a few days after admission the enlargement of the liver disappeared, as did also the cyanosis of the extremities; the edema diminished, but has never entirely disappeared. The urinary findings two and a half months after the disappearance of all signs of circulatory insufficiency were practically unchanged.

Table I gives the results of the routine urinary examination:

TABLE I.

Date.	Amount.	Specific gravity.	Reaction.	Albumin, grams per liter.	Hyaline casts.	Granular casts.	Fatty casts.	Epithelial casts.	Cylindroids.	Red blood corpuscles.	Epithelial cells.	Free fat.
July 1	1025	Alk.	4	Many	Many	Many	...	+	Few	+	+
July 7	1019	Acid	Cloud	+	Many	Many	...	0	0	Few	+
July 9	970	1019	Acid	3	+	+	+	+				
July 15	790	5	Many	Many				
July 27	1350	1012	Acid	2.7	Many	Many	Many				
Aug. 7	1600	3	Many	Many	Many	Many	+
Aug. 15	1007	Acid	Cloud	Few	Few	Few	Few	+
Aug. 16	Cloud	Many	Many	Many	Many	Few	
Aug. 27	1013	Acid	Cloud	Many	Few	Few	
Aug. 30	2170	1011	2.5	Many	Many	Few	Few	
Sept. 10	1017	Acid	3.7	Many	Many	Few	
Sept. 30	Acid	Cloud	Many	Many	Few	
Oct. 3	1600	1013	Acid	4	Many	Many	Few	
Oct. 6	1030	1019	Acid	5	Many	Many	Many	Many	Few	

In view of the evidence of definite nephritis, studies of the functional efficiency of the kidneys were instituted. The phthalein test was twice performed according to the technique of Rowntree and Geraghty. The following surprising results were obtained:

July 5. Elimination after one hour, 50 per cent.; after two hours, 71 per cent.

September 14. Elimination after one hour, 67 per cent.; after two hours, 82 per cent.

The indigo-carmin test was done on July 15, and the dye was seen coming from each ureteral orifice at the end of six and one-fourth minutes. Both of these functional tests showed, therefore, unusually prompt elimination.

Studies were then made of the chloride and nitrogen elimination

after the addition of known quantities of sodium chloride and of urea to a constant diet. The patient was put on a salt-poor soft diet, with constant quantity of milk and 7 grams of sodium chloride every twenty-four hours, beginning September 16; the sodium chloride was increased and urca added to the diet as indicated in Table II. The total elimination of chlorides was estimated by the Volhard-Arnold method, and of nitrogen by the Kjeldahl method. (Sec Table II.)

TABLE II.

Twenty-four hours beginning	Amount of urine in c.c.	Specific gravity.	Albumin by Esbach. Grams per liter.	NaCl added to food.	NaCl in urine.	Nitrogen in urine.
Sept. 19	1520	1.013	6	7 grams	7.9	
Sept. 20	1220	1.013	7	7 grams	6.8	
Sept. 21	1100	1.016	7	7 grams	7.3	
Sept. 22	1520	1.016	6.5	10 grams	10.03	
Sept. 23	1380	1.016	6	20 grams	13.1	11.35
Sept. 24	1530	1.014	5.5	20 grams	16.9	11.85
Sept. 25	1375	1.015	7	7 grams	14.3	11.8
Sept. 26	1500	1.017	8	7 grams	12.6	15.0 Given 10 grams urea by mouth = 4 grams N.
Sept. 27	1350	1.018	7.5	7 grams	12.1	12.1
Sept. 28	1540	1.014	6	8.3	9.4

These results show no delay in the nitrogen elimination and fair elimination of sodium chloride. There is, however, some delay in the elimination of the larger amount of sodium chloride given, and this, together with an increase of edema on the days of high chloride administration, which promptly subsided during the next few days, is suggestive of beginning impairment in the chloride tolerance. It is not to be understood that the patient was on a perfect salt balance in this experiment.

Although recent work would indicate that the phthalein test is the most reliable single test of renal efficiency, we have apparently occasional cases of nephritis, as that presented, in which beginning impairment in the chloride-eliminating capacity of the kidney is evident at a time when the phthalein elimination is still unusually prompt.

A second case that seems worthy of mention gives the following history: At the age of six years the patient, a male, had an attack of scarlet fever followed by edema. Good health returned and continued for ten years, until, at the age of sixteen, he developed an abscess in the left iliac fossa. This was opened and drained. Following the operation general anasarca of a severe grade developed, and a fatal termination seemed imminent. A bilateral decapsulation of the kidneys was followed by improvement, and the patient left the hospital in good condition four months later.

His health has been good for three years since, except for short periods of renal inadequacy every four to eight months. At these times he exhibits edema and some decrease in the amount of urine. He recently returned to the hospital in one of these attacks. Examination of the urine showed 2 grams of albumin per liter, many and various casts, and some blood. However, after but a few days of treatment, with improvement, his phenolsulphonc-phthalein elimination was 46 per cent. in the first hour and 23 per cent. in the second hour, a total of 69 per cent., or approximately normal. Here again the phenolsulphoncphthalein elimination cannot be considered a true index of the health and efficiency of the kidneys.

The third case of interest was one of bilateral polycystic kidneys. The patient, a man, aged forty-two years, under observation for two weeks previous to death, had been in good health until about a month before admission. He then began to suffer with pain in the lumbar region and hematuria associated later with vomiting and other symptoms of uremia. He was admitted to the hospital in September, 1912, and at this time presented evidence of an infection, that is, a septic temperature running as high as 103°, with occasional chills. The amount of urine passed was fairly abundant, ranging from 800 c.c. to 1000 c.c. per day. Urinalysis at first revealed a low specific gravity, little albumin, and no formed elements, later the albumin increased and many hyaline and light granular casts appeared, with finally numerous erythrocytes.

The phenolsulphoncphthalein test was performed twice, thirteen and eleven days before death. At each test the elimination in two hours was an unmeasurable trace, though the elimination of the dye in traces continued for about eight hours. Up to the last day before death the elimination of water by the kidneys was quite free and the chlorides and nitrogen of a restricted diet were approximately completely eliminated. Accurate metabolic studies could not be made because of vomiting, but the elimination in the urine in twenty-four hours was for several successive days from 2.64 to 4.3 grams of sodium chloride and 4.4 to 5 grams of nitrogen. The development of uremic symptoms steadily progressed, ending in death. At autopsy the clinical diagnosis was confirmed by the finding of large polycystic kidneys, in which almost no renal tissue could be found. The symptoms of infection were explained by a suppurative process in the bile passages, associated with gallstones and multiple abscesses of the liver. It is of interest that small cysts were found throughout the liver, a finding probably to be correlated with the polycystic kidneys.

Rowntree and Geraghty make note of a patient with hypertrophied prostrate and normal phthalein elimination who died later of pneumonia, and at autopsy was found to have bilateral

polycystic kidneys. The phthalein test, however, showed no evidence of renal insufficiency.

These two findings in polycystic kidneys tally with the clinical picture in this disease, renal function being apparently adequate for years until some intercurrent infection causes impairment, and eventually uremia and death.

Rowntree's case of polycystic kidney is an example of good elimination before, and ours of faulty elimination after, the intercurrent infection.

This brief report is presented for the purpose of calling attention to certain interesting phases of phthalein elimination, and with no intention of minimizing the importance of the test, which, on the contrary, we believe to be of the greatest value for the determination of renal efficiency.

PRIMARY ADENOMATA OF THE LIVER SIMULATING HANOT'S HYPERTROPHIC LIVER CIRRHOSIS.

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ADENOMATA of the liver are rare, and only the most meager mention of these tumors can be found in our recent text-books or systems of medicine, or even in our standard works on pathology. From the literature we have been able to collect but 44 cases of this condition, 16 of which were solitary, and 28 multiple. Of the latter 28 there were 21 associated with the atrophic cirrhosis of Laennec and the remaining 7 had no mention of any cirrhosis whatever. These primary cases were accidental discoveries at autopsy, and no reference was made to any symptoms which they may have induced. In 25 of the 44 cases the tumors were composed of modified liver parenchyma, and in 19 the structure was that of agglomerations of large bile ducts. Of these 19 there were 4 multiple and 15 solitary.

The greater portion of these cases were unaccompanied by any sort of clinical history, and were apparently collated for the sole purpose of the statistics of incidence.

In his book *Diseases of the Liver*, Rolleston devotes some space

to the consideration of adenoma of this organ. He divides all adenomata into three classes: (1) Composed of or derived from the ordinary parenchymal cells; (2) those derived from the bile ducts; (3) those due to the inclusions of adrenal "rests." Since the case herewith reported comes under the first class we will confine our attention to it alone.

In common with all who refer to the condition at all, Rolleston holds that the majority of instances of multiple liver adenomata are associated with and secondary to cirrhosis of that organ, the condition being essentially a compensatory process of cell hypertrophy to offset the destruction of the parenchyma by the disease. He regards them as "exaggerations of the hobnails seen in portal cirrhosis," and states that they are to be explained as a final stage of this nodular hyperplasia. Necrosis, fatty metamorphosis, and portal thrombosis are particularly apt to follow. On the other hand, Engelhardt ascribes their etiology to a toxin which has been producing the connective-tissue hyperplasia of the cirrhosis and is supported later in this view by Dieulafoy. The toxins of malaria have been known to produce adenoma of the liver, and injections of toxins resulting from blastomycetic infections have produced the same result. In favor of the compensation theory, it may be mentioned that in the portal cirrhotics where the cell destruction is most marked the majority of instances of adenoma occur, while in the types of cirrhosis which are characterized by long preservation of the liver cells it never occurs.

A very common fate of adenoma of the liver is their malignant transformation into carcinomata, according to Sabourin, who has written extensively on this phase of the subject. This is usually fairly early in the history of the adenomatous condition, and is nearly always accompanied by infiltration of the portal vessels, with consequent tumor-cell emboli, by spread to the other surrounding structures, and by metastasis to various tissues by way of the lymphatics.

According to Rolleston and emphasized by Engelhardt, in nearly all of the cases of multiple adenomata there is associated with the cirrhosis a thrombosis of the portal vein, and consequently a high percentage of these tumors are marked by the vomiting of blood and by ascites.

Many of the foregoing data are of interest in the light of the case here reported, and are, therefore, selected for mention.

CASE HISTORY.—The patient, C. M. H., aged thirty-one years; married; occupation, paper-box manufacturer. First consulted one of us on May 31, 1906, complaining of weakness, loss of appetite, pain, dragging in the abdomen, and jaundice.

He has had all the infections of childhood, since which time he has been in perfect health until about two years ago, when he developed what was then diagnosticated as a severe attack of

influenza. He dates his present illness from that attack, never having been well since. He denies all venereal disease. He has never been in the tropics, and has never suffered from malaria or dysentery. His habits are of the best. He uses no tobacco or alcoholic stimulants. He complains of weakness, dragging, and fulness of the abdomen, dull pain in the back and loins, and loss of appetite. He states that he has had several attacks of feverishness for which he could not account. He has never bled from the gums, nose, stomach, or rectum. He never suffers from headache, and his bowels are regular. The stools, he states, are light yellow in color, and he has never observed them clay colored. His urine is abundant, dark in color, and deposits much brick-dust sediment. He has noticed that the jaundice from which he suffers fluctuates in intensity. Sometimes his skin is extremely dark and at other times much bleached.

EXAMINATION. The patient is a well-built man, his muscles are flabby, and the visible mucous surfaces are pale. His skin and conjunctivæ are universally and deeply bile-stained. There is no edema or cyanosis. His respirations are quiet and the pulse slow. The skin is dry and a little harsh.

Lungs: Apart from a moderate degree of emphysema they seem normal.

Heart and Arteries: The cardiac impulse is visible in the fifth interspace 8 cm. to the left of the midsternum. No friction or thrill over the precordium exists. The cardiac dulness is nearly effaced by a hyper-resonant note. There is a soft basic systolic murmur slightly conducted into the carotids and also heard over the pulmonic and aortic interspaces. A soft systolic apical murmur is heard, conducted feebly to the left. The pulse is 60, regular, soft, and easily compressed. The systolic blood pressure is 130 mm. of mercury; the diastolic pressure, 80 mm.

Blood: Red cells, 3,250,000; white cells, 8000; hemoglobin, 70 per cent.; color index, 1. The red cells presented no nucleated forms and no poikilocytosis. No malarial parasites seen. The staining reaction was good.

Abdomen: The whole upper half of the abdomen is full and prominent. There is a slight right inguinal hernia, easily reducible. There are no enlarged veins traversing the abdomen or chest; no dulness exists in either loin or in the dependent parts of the abdomen when standing. The kidneys are not palpable.

Liver: The dulness of the right lobe of the liver in the mid-clavicular line extends downward from the level of the fifth rib 18 cm., while that of the left lobe extends downward from the sternoxiphoid articulation 20 cm. The liver border is rounded, firm in consistency, painless on pressure, and has no palpable nodules. A deep notch, easily palpable, separates the large and heavy left lobe from the right. Another deep notch exists in the

position of the fissure of the gall-bladder. The latter organ, however, is not palpable.

Spleen: The dulness of the spleen extends from the seventh rib downward and forward, whence it apparently blends with the dulness of the left lobe of the liver. Its lower border is firm and smooth.

Rectum: Examination of the rectum showed no hemorrhoids. The prostate gland was normal in size and consistency and perfectly smooth.

Glands: No enlarged lymph glands were detectable. There was no joint or bone tenderness.

Nervous System: Examination of the nervous system was entirely negative. The ophthalmoscope showed no changes in the optic disks or retinae.

Urine: Twenty-four-hour specimen; amount, 3 pints. Reaction, acid; color, dark amber; specific gravity, 1022; foam, bile-stained. All tests for bile, positive. No albumin or sugar; no indican. There are a few bile-stained casts. No blood cells discernible. Amorphous urates in abundance.

The stool was light yellow in color and soft in consistency. It contained no mucus, amebæ, blood, or other pathogenic parasites.

He was again examined in April, 1907, and the following notes taken:

Jaundice much more intense. Slight soft edema about the tibiæ, no cyanosis, slight general emaciation. The left lobe of the liver almost fills the upper half of the abdomen, extending downward two fingers' breadth below the umbilicus. The right lobe, though very large, appears much like an appendage to the left. The spleen, owing to the large left lobe of the liver, is palpated with difficulty. No enlarged veins are visible and no signs of free fluid exist in the peritoneal cavity. No hemorrhoids are present. Systolic, basic, and apical murmurs are present. The systolic blood pressure is 120 mm. of mercury. The blood picture is that of a secondary anemia. The stools are light though not clay colored. The patient states that the stools change their color from time to time. Physically, he is much weaker, has a fickle appetite, and suffers from great itching of the skin and from insomnia.

He was observed from time to time during the year 1907, but no remarkable change in his condition was found. His jaundice would fluctuate; at times he would become dark and again much lighter. His stools, while not clay-colored, were much lighter than when he first came under observation. He resided in the country and remained in fair health until the fall of 1908, when all his symptoms became much worse: his jaundice was intense, his stools about clay-colored, his urine scanty and full of bile, his gums vascular and bleeding on the slightest provocation, but without hemorrhage from any other mucous surface. His liver remained about as described above,

the left lobe always being the most prominent. There was no evidence of portal obstruction. A week before his death, however, changeable dulness was detected in each flank, but not enough fluid existed to produce a fluctuation wave. A few days prior to death he became delirious, drowsy, gradually passed into deep coma, which lasted about forty-eight hours, and died.

The complex of symptoms presented during the course of the disease were: (1) A long, continuous jaundice fluctuating in intensity; (2) a gradual but progressive liver enlargement until it became of enormous size, with special prominence of the left lobe; (3) definite though moderate enlargement of the spleen; (4) absence of acholic stools until within a few days of death; (5) absence of ascites, hemorrhages from mucous surfaces, or enlargement of the abdominal or hemorrhoidal veins; (6) presence of attacks of abdominal pain, with febrile reaction; (7) abundant bile-stained urine; (8) cholemia and death.

The presence of the above complex naturally led to a diagnosis of hypertrophic biliary cirrhosis of the type of Hanot. Owing to a moderately well-developed panniculus, and also to the fact that most of the tumor masses located on the ventral wall were small, the nodules were not palpable.

AUTOPSY. Mr. C. M. H. Performed by Dr. H. W. Carey, March 8, 1908. Autopsy No. 105, from the Samaritan Hospital records.

The body is that of a well-nourished man, 170 cm. in length. There is marked jaundice of universal distribution, together with much staining of the conjunctivæ. The pupils are equal. The abdomen is slightly distended and full in the flanks. There is slight edema of both ankles. Rigor mortis is well marked. There are no enlargements of the superficial lymph glands. The superficial veins are not enlarged. The body has been embalmed.

The peritoneal surfaces are normal save for a line of adhesions along the course of the urachus to the coils of the intestines above the pubes. It contains no dilated veins. The appendix is normal. The coils of intestines are normal.

On raising the costal flap no enlargement of the internal mammary veins is noted.

The lungs are normal except for two small infarcts on the lower border of the right lower lobe. There is slight edema and congestion of the lower lobes of both.

The bronchial glands are normal.

The pericardial sac is normal.

The heart shows considerable thickening of the aortic valve, due to vegetations on the proximal side of the leaflets, which narrows the valvular orifice and renders the valve as a whole, incompetent.

The spleen is about normal in size and weighs 645 grams. It is

negative throughout. Nearby in the omentum are two small accessory spleens about 1 cm. in diameter, but presenting nothing unusual in their structure.

The stomach is normal.

The pancreas is normal.

The kidneys are normal save for a marked pallor and indistinct markings in the right.

The adrenals are normal. There are no signs of tumor growth seen.

The intestines, bladder, genitalia, and bone-marrow are normal.

The liver: On opening the abdomen the lower border of the liver presents in the midline 11 cm. below the tip of the ensiform cartilage. On removing the chest wall the portion first visible is seen to be the left lobe, the right lobe being pushed well into the right flank and encroaching above upon the right pleural cavity. On removal of the liver it is found to weigh 2445 grams (5.3 pounds).

In color, the liver is nearly all of a peculiar yellowish green, but a small portion is fairly normal purplish red. The whole surface is broken up into literally innumerable nodules, leaving no part of the surface smooth. Over the upper surface these are approximately 1 mm. to 1 cm. in diameter, while on the under surface most of them are much larger, measuring from 2 cm. to 3 cm. These nodules, where not bile-stained, are dark purplish red and do not show the light yellowish or bleached appearance common to fatty deposits in nodular livers. The interstices between the nodules are not rich in fibrous tissue nor are the depressions so sharp as in the surfaces of atrophic cirrhosis. In some places the capsule is thickened, but for the most part it is surprisingly thin considering the evident abnormality. On section the entire liver is found to be divided into thousands of small round masses of sizes varying about as the nodules upon the surface. Nothing approaching the appearance of normal liver tissue is identifiable to the naked eye. The consistence of these masses is firm but by no means hard. The liver as a whole, is somewhat firmer than normal but has not that absolute leathery feeling common to advanced cirrhosis. The cut surface of the nodules seems somewhat paler than the nodules appear on the outer surface, whether they are bile stained or not. Each mass seems to be surrounded by a fine connective-tissue capsule.

The gall-bladder wall is much thickened, but the mucosa, though pale, is normal in appearance.

The portal veins are clear throughout. No thrombi or other obstructions and no dilatations are found in them or their tributaries.

MICROSCOPIC DESCRIPTION. The lungs are normal except for the presence of the infarcts and slight congestion and edema.

The heart muscle is normal.

The spleen shows a slight chronic interstitial splenitis. The two small accessory organs have a normal splenic structure.

The kidneys: The right shows slight hemorrhage. The left is normal.

The mesenteric lymph nodes, stomach, and intestines are normal.

The liver: The blocks of tissue studied were fixed in formalin. The paraffin, celloidin, and freezing methods were used. The sections were stained in hematoxylin-eosin, eosin-methylene blue, Mallory's connective-tissue stain, v. Gieson's stain, safranin, phosphotungstic acid hematoxylin, and scharrlach R.

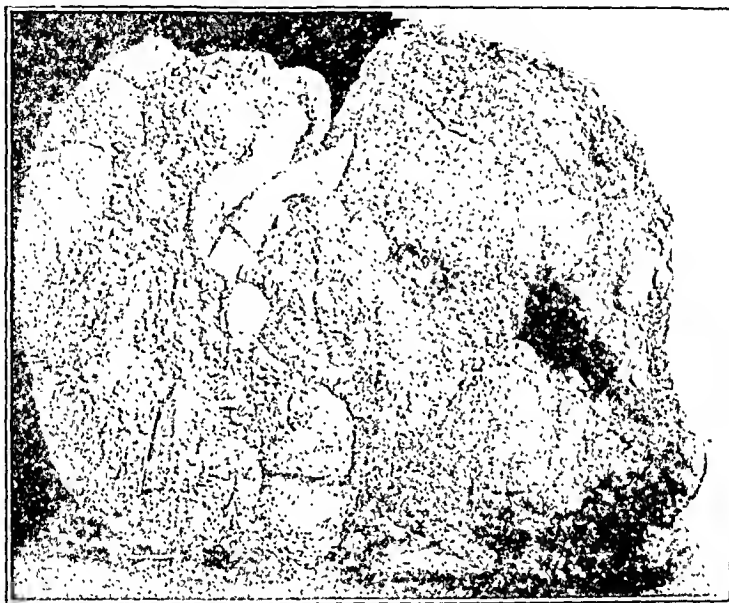


FIG. 1.—Adenoma of the liver, showing under surface. Note large size of the nodules and the great enlargement of the left lobe.

As the sections from the different portions of the liver are gradually gone over, the first point which impresses one is the almost total absence of normal or even relatively normal parenchyma. In its stead one sees a picture composed of generally round masses of cells of different sizes, each surrounded by a definite capsule. At first one is inclined to believe each mass derived from an original lobule of the liver, but on closer inspection, this structure is nowhere definitely preserved. Sometimes one sees what appears to be the remnant of a central vein but in most cases even this is absent. An occasional portal space has survived the change sufficiently to be recognizable. The arrangement of the cells corresponds in places to that of the normal parenchyma, but the likeness is limited, however, to the fact that the cells form minute bile ducts, and seem to be disposed about a lumen which in some instances is apparently filled with a cast composed of closely

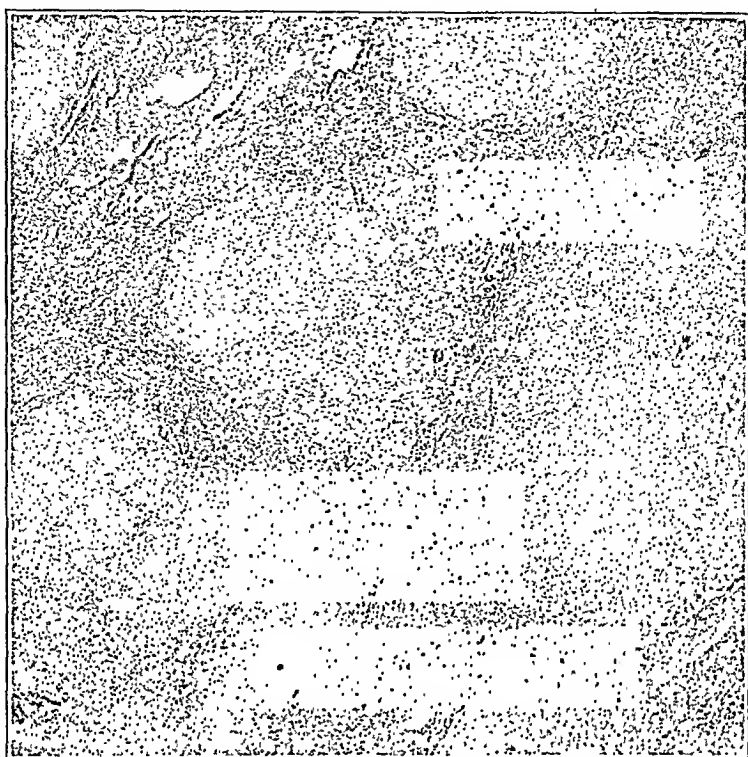


FIG. 2.—Adenoma of the liver ($\times 70$). Single eneapsulated nodules. At lower left corner are parts of four lobules coalescing to form a new adenoma nodule.

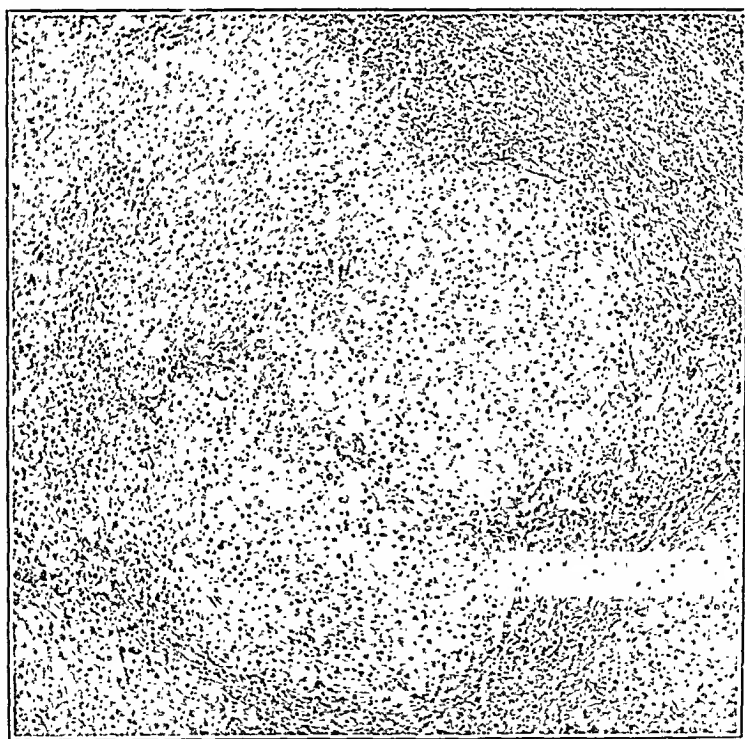


FIG. 3.—Adenoma of the liver ($\times 200$). Same location as in Fig. 2. Cells brought out more clearly.

packed masses of pigment granules and detritus. In the majority of cases the cell masses are mere groups with no definite arrangement like that of the liver cells. They are noticeably poorly supplied with bloodvessels for the most part. Some, however, have quite a number of small twigs running along between the duct-like strands of cells (Fig. 4). In all instances they arise from the capsular vessels.

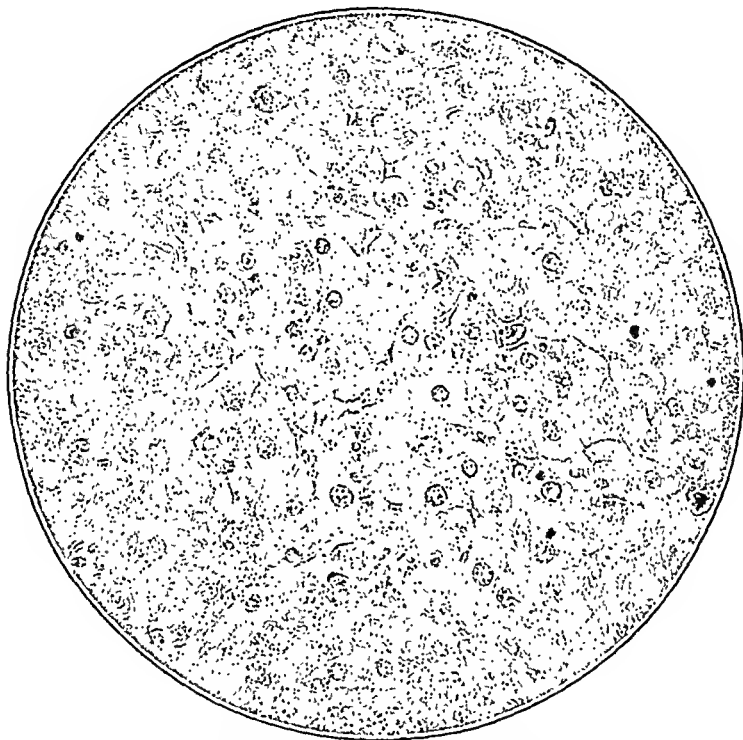


FIG. 4.—Adenoma of the liver ($\times 800$), showing details of the cells and their likeness to the normal cells of the liver. Note the double nucleation of some of the cells and the pigment casts of the ducts.

The cells are polygonal in shape, but not as sharply polygonal as are the normal cells. These tend to be rather more rounded and irregular. No columnar cells are seen, neither are there any reversions to embryonic type. The characteristic cell is much larger than that of the liver cell, and may be three or four times its size. Usually their size is definite for a certain mass, one mass containing only large ones, while another is made up of much smaller cells. The size of the cells is generally much greater than usual in sections taken from the deeper portions of the organ and coincidentally the deposit of pigment in the cells and between them, which is widely distributed, is much more prominent in these deeper portions. The pigmentation is in the form of granules of coarse and finer sizes which often packs the cells to such an extent that their morphology is totally obscured. It is partly

hematogenous and partly biliary in origin, the hematogenous granules coming out clearly by the ferrocyanide-HCl test in frozen sections.

The cells when not obscured by pigment show a clear, homogeneous protoplasm, and with some stains, particularly v. Gieson's, the cell body takes on an almost glairy appearance. The protoplasm takes a light pink stain with eosin-methylene blue and a slightly darker hue with hematoxylin-eosin. In the sections stained by v. Gieson's stain there is marked variation of the protoplasmic stain, those cells in what seems the older portions taking the lightest coloring and some having totally lost their staining capacity. The cells rest on a delicate basement membrane, which stains clearest in the phosphotungstic acid hematoxylin preparations. No intercellular bridges of any kind are seen.

The nuclei are uniform in size, irrespective of the size of the cells. They take a pale blue stain in the eosin-methylene blue preparations and show no marked chromatin network. A good number of cells are doubly nucleated, and in these the daughter nuclei are darker than the others, and have a more decided chromatin network. Wherever it can be determined, these nuclei have always divided by simple fission. The very few examples of karyokinesis observed in the safranin-stained sections do not show any remarkable characteristics.

The masses of cells are surrounded by strands of connective tissue of moderate thickness and density. Near the junction of several of these cell groups the areas of connective tissue are of considerable extent, and, indeed, throughout the sections the amount of connective tissue and its arrangement at first suggest cirrhosis. With closer study some facts appear which seem in our judgment to controvert this idea. In the first place the lobule of the liver as such is not the histological unit giving rise to these growths. In the multilobular or Laennec's type of cirrhosis we see small groups of lobules surrounded by bands of connective tissue, the latter conforming more or less closely to the outlines of the lobules in the group; nevertheless we never see the connective tissue splitting up several lobules, including half the resulting divisions in a single group and entirely leaving out the other portions. In this case, however, there appears to be a somewhat analogous process going on. There are certain areas where the adenomatous transformation is not complete. In these instances there is apparently a centre of transformation in one portion of a lobule from which the adenomatous change gradually spreads, slowly involving parts of neighboring lobules. The capsule forming about this newly evolved growth creeps around the adenomatous portions and merges them into one mass, the other and normal portions remaining outside the capsular wall.

Again, of the two processes, cellular growth and connective-

tissue proliferation, the latter seems relatively much younger and is certainly much younger than a like amount of cirrhotic connective tissue. Only in the deeper and older portions of the growth is there any density and tendency to hyalinization, and in contradistinction to this the cells in these locations show disintegrating nuclei, poorly and unevenly stained protoplasm, which is often hyaline, and even large areas that have undergone degeneration and become necrotic. Nor do we see the bile-duct formation to anything like the extent seen in nearly all cases of cirrhosis approaching this grade of connective-tissue formation. In places one sees areas of relatively normal but greatly compressed liver cells. That these are groups composed of many lobules can be easily seen, and here it is noteworthy that the connective-tissue growth is entirely absent, the compression being the result of the pressure of the surrounding cell masses and their capsules.

Nowhere in the sections do we see any intercellular or intra-lobular connective-tissue invasion except to the slightest extent. Such invasion as can be seen is brought out only by the special connective-tissue stains.

There are several areas, as above mentioned, where it is possible to see a direct change in the parenchyma from the normal to the adenomatous type. It is significant that the connective-tissue capsules surrounding them are rudimentary in comparison to the capsules of the older growths. In these newer portions the connective-tissue cells are younger and more nearly of the fibroblastic type, and there is no hyaline change visible. The amount of the fibrous proliferation seems proportional to the completeness of the transformation to the adenoma structure.

In the larger areas of connective-tissue formation one sees many large and small bile-ducts which in most cases are dilated. They are lined by cuboidal epithelium, and in many instances are filled with great masses of granular pigment of biliary origin.

No tendency to malignant transformation is anywhere noted. No new growth of any kind is seen anywhere else in the body.

We have here, then, a case of adenoma of the liver whose multiple nodules have replaced the liver substance to such an extent that only microscopically can any normal liver tissue be found. They are derived from the liver parenchyma itself, instances being seen of transformation in progress. Each tumor nodule is encapsulated. That this connective tissue is not the manifestation of a cirrhosis is demonstrated by: (1) Individual nodules do not spring from original individual lobules; (2) parts of many lobules are united in some instances to form the tumor nodules; (3) where the neoplastic transformation is in progress we find these parts surrounded by only rudimentary capsules; (4) the few areas of normal though compressed liver tissue visible are not invaded by a connective-tissue overgrowth such as one would expect if the condition were

one of cirrhosis; (5) there is no fatty metamorphosis, malignant transformation, other tumor formation or any abnormality of the portal veins.

The case herewith reported is of interest because (1) it presented the symptom complex of Hanot's hypertrophic biliary cirrhosis; (2) because the study of the liver does not bear out the generally accepted view that multiple adenomata are always secondary to and in compensation for liver cirrhosis; (3) because it shows the importance of recognizing the fact that symptoms identical with those produced by either the atrophic or the hypertrophic form of cirrhosis may take their origin from multiple adenomata.

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REVIEWS

DIGESTION AND METABOLISM. THE PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY OF NUTRITION. FOR STUDENTS AND PHYSICIANS. BY ALONZO ENGLEBERT TAYLOR, M.D., Rush Professor of Physiological Chemistry, University of Pennsylvania, Philadelphia. Pp. 560. Philadelphia and New York: Lea & Febiger, 1912.

BEARING the signature of one of America's greatest exponents of the philosophy of science, this book by Taylor deserves a careful perusal by its readers. Let not the student or physician for whom this book is written, sigh hopelessly as he buffets with lusty sinews the raging scientific tenet of the first two chapters, for it is in these two chapters that the most difficult channels are found. Even the modern student (for we understand Professor Taylor to mean the undergraduate) with the advantage of the newer scientific training, will find the reading of these two chapters a most arduous undertaking, but the physician, and we understand his prototype to be the practitioner, will we fear, not trust himself to embark on such a flood. These two chapters to the reviewer's mind, are the most difficult of comprehension. Dr. Taylor, whose work with ferments needs no mention, treats his favorite theme in a manner as clear as is the question of fermentation itself, and therefore he bewilders us. His grasp of the subject is no doubt firm, but his exposition thereof is obscure at times, due we believe to his thorough knowledge which presupposes students and physicians to be in lesser degree, as fundamentally well informed as is he himself. In justice to the author, we must express our conviction that the abstruseness which we find, is due mostly to the recondite nature of the subject. Furthermore, we must acknowledge that few authors could so adequately depict the *modus operandi* of catalytic acceleration or fermentation.

The chapters on "Digestion" and "Metabolism" (*in toto*) are those on the metabolism of certain food stuffs, are excellently penned, and are pregnant with information bearing the hall mark of the writer's great experience. For instance, sound argument against the use of indoxyl, conjugate sulphates, and other waste products, as an index of intestinal putrefaction, is offered in such a form that refutation of Taylor's views seem impossible. We

have read much on this subject, but nowhere is it handled so clearly in a few words as by Taylor. We admire also the chapter on autointoxication, a name which has been so grossly misused as "to have lost concrete meaning," but regret, although the subject does not lie within the scope of this treatise, that the chapter should have been so curtailed.

To discuss in detail the many admirable features of this work, would mean more space than is allotted to this review, for the book is replete with valuable information, now easy of acquisition, a fact which must be regarded by all as a notable educational accomplishment. One must not estimate this volume as a text-book this it is not, and cannot be; but to the student (and the reviewer now applies this term in its broadest sense) who desires authoritative information on problems of digestion and metabolism it is especially recommended.

The work is distinctly original in conception and execution, and in this it differs uniquely from many of the too numerous scientific books. It represents an individuality and not alone a compilation, thereby giving the impression of something new and not merely an inheritance, thus acquiring an authoritative atmosphere which one somehow misses in most works. We felicitate the author on this notable result of his labors, and prophesy for it a distinct place in American scientific literature. E. H. G.

INTERNAL MEDICINE. By DAVID BOVAIRD, JR., A.B., M.D., Assistant Professor of Medicine in the College of Physicians and Surgeons of Columbia University; Associate Visiting Physician of the Presbyterian Hospital, and Visiting Physician of the Seaside Hospital, in the City of New York. 109 illustrations and 7 colored plates. Philadelphia and London: J. B. Lippincott Company.

BOVAIRD's book attempts to compress into less than 600 pages the whole of the subject of the practice of medicine. It holds, therefore, in size, a relation midway between the undesirable and now happily less popular compends and the large single volume medical works of which there is such a surfeit on the market. Despite the condensation all the essentials are to be found in the book, so that the student in particular will find it useful in preparing for his final examinations. But he must not think, as he is inclined to do, that he has covered the subject of medicine when he has read Bovaird's book or one of similar size. Such books, as well as the smaller compends, often create a false feeling of thoroughness. The student, it seems to the reviewer, should be urged to read important subjects, whether in internal medicine or in

surgery, in monographs, at any rate in one of the large medical works, so as to acquire a broader viewpoint and a little knowledge of the history of the particular subject he is studying. The reading of a compend or a book like Bovaird's cannot supply these desiderata.

The author's diction is good except that he has no mercy on infinitives and splits them ruthlessly. The appendix on the care of the sick and on diet add much to the usefulness of the book.

D. R.

PRINCIPLES OF HUMAN PHYSIOLOGY. By ERNEST H. STARLING. M.D. (Lond.), F.R.C.P., F.R.S., Hon. M.D. (Breslau), Jordell Professor of Physiology in University College, London. Pp. 1423; 564 illustrations. Philadelphia and New York: Lea & Febiger, 1912.

IN these times of overpublication the teacher of physiology is prone to look upon each new text-book on this subject as another useless product of the efforts of a physiologist unconsciously stimulated to the work by the keen business methods of one of the many publishers. Of the scores of text-books in this field less than a half-dozen have a justification for their existence. To write a satisfactory work of this kind requires an extremely broad as well as detailed knowledge of the subject in all of its branches, and at the same time a long teaching experience. Few men have these qualifications in this age of investigation which concentrates the attention upon one part of the subject. Investigators, when writing text-books, usually give entirely too much space to the subjects in which they are particularly interested. The finished product is consequently unbalanced. However, even a hasty survey of the latest book of Starling convinces one that the author has all of the qualifications of a successful writer of text-books. Upon closer perusal this opinion is justified in every respect. A reviewer is prone to read critically first of all those chapters which contain subject matter with which he is most familiar, but here the book stands the severest test. Again, when he turns to the chapters which contain the discoveries of the author he finds no material which is not of value to the student even though not specializing in physiology. The author shows an immense grasp of the subject, and combines with it a capability of clear description which makes every part of the book interesting.

The book is quite large, consisting of over 1400 pages, but one feels that it is not too large. Every page contains material which the earnest student will be interested to know. Nor would the practitioner, referring to the book upon any subject whatever, be satisfied with less than the author gives him. One cannot under-

stand why Starling could have felt the necessity of a manual such as he wrote a few years ago. It was an excellent work, but too brief for these times in which physiology has come to occupy such an important and extensive position in biology and medicine.

In his last work, methods receive much more attention than is accorded them in other books of equal size, but this seems justifiable as the practical work in physiology which is given to the student in every good school, has created a desire among students not only to know that a thing is so, but also how it has been demonstrated. One shortcoming is the absence of references in the text which often is so convenient to the student who wishes to learn more of a subject.

After a brief introduction the author takes up the chemistry of the constituents of the organism in a brief yet thorough enough manner. This is followed by a chapter on the energetic basis of the body which contains much of the important material contributed to physiology by physical chemistry. The chapter is thoroughly up to date. The following subjects are considered: The energy of molecules in solution, passage of water and dissolved substances across membranes, the properties of colloids, the mechanism of chemical changes in living matter, and the electrical changes in living tissues. With this the author plunges at once into special physiology, considering first the mechanism of movement and sensation. Then nutrition in all of its phases is taken up, and finally reproduction. The chapter on the ductless glands is excellent. The physiology of pregnancy and reproduction is given more space than is usually allotted to this subject. Each chapter so far as the reviewer can judge, is well balanced, contains well selected material and clear descriptions.

E. L.

DEFORMITIES, INCLUDING DISEASES OF THE BONES AND JOINTS.
A TEXT-BOOK OF ORTHOPEDIC SURGERY. By A. H. TUBBY,
M.S. (Lond.), F.R.C.S. (Eng.). Second edition. Vol. I; pp. 883;
603 illustrations. Vol. II; pp. 867; 483 illustrations. London:
Macmillan & Co., Ltd., 1912.

THERE has been an increasing ambition in many of the physicians who have devoted their attention to orthopedic surgery, to produce a book on the subject to serve at least four purposes: (1) As a text-book for students; (2) as a reference book; (3) to bring together in a logical sequence the maladies which belong to the specialty, and (4) to emphasize the writer's views on conditions which absorb his especial interest. General and comprehensive collections of orthopedic facts have not been, nor could they be, entirely satisfactory. The scope of orthopedic surgery

can be fairly clearly defined if it be approached in the proper spirit. Orthopedic surgery should embrace defects common to the body mechanisms upon which position, motion, and locomotion depend. Freely abridging the subject, and the inclusion of conditions which do not belong to the specialty, should be reckoned with as faults. Tubby's work approaches to a gratifying degree the needs that have been keenly felt by the more advanced students in orthopedic surgery. It is too comprehensive for the academic student, it would confuse and encumber his first skeletal notions of the subject. Some of the cuts are crude and do not emphasize the topic discussed. Many of them are especially noteworthy. The two volumes of the work contain over 1000 cuts, 400 of which are original. Due credit is given to the authors of borrowed cuts, as well as to authors of ideas as to treatment and technique.

The logical and etiological arrangement of the subject matter has received very careful attention. The context is to the point, although there are a few instances where verboseness can be charged, yet clearness and finish do not suffer seriously. A vein of optimism is felt which adds encouragement but which carries a danger of imparting prejudice.

In this work there is not an offensive evidence of the author at every turn, nor is there an undue prominence of his views. It brings together the research, experiments, and experience of the leading orthopedic surgeons of the world in a very gratifying fashion; it is rich in bibliography. There is generally a pleasing diversification of opinion and methods of practice. Pathology and pathological anatomy have received a creditable amount of attention.

Conclusions are augmented by facts from the author's and other men's hands, varying results are given frequently, which favor unbiased opinions.

The thought that there is a lack of predominating originality arises in one's mind as he inspects the work, its creation, however, entailed an enormous amount of labor for the author and his collaborators. Too much credit cannot be given for the indefatigable energy with which the author pursued his task in compiling this diversified and orderly work.

W. J. M.

SEXUAL IMPOTENCE. By VICTOR C. VECKI, M.D., Mt. Zion Hospital, San Francisco. Fourth edition. Pp. 394. Philadelphia: W. B. Saunders Company, 1912.

THE fourth edition of this book is revised and enlarged. It is written in a clear and bold style, and is stamped with the author's

individuality. The chapters on anatomy, and especially physiology, are more complete than one usually finds in a work of this kind. In considering the etiology of impotence the author recognizes the difficulties of classifications upon scientific basis, and divides the various causes into seven groups for convenience of description. One-half of the work is devoted to the various causes under no less than eighty-two headings. Masturbation, resulting in morbid pollutions and spermatorrhea, is regarded as the essential cause of impotence. The injurious effects of sexual excesses on the functional capacity of the sexual organs are considered more exaggerated than underestimated, and excessive continence may result in constitutional and sexual injury. Gonorrhea, its complications and sequelæ, conceded by many urologists to be of considerable importance in the etiology of impotence and allied sexual derangements, receives scant attention. In considering the treatment many drugs are discussed, and due attention paid to hydrotherapy, electrotherapy, organotherapy, mechanical devices, and general constitutional treatment. Local treatment is recommended when indicated, and a wise protest is entered against too severe urethral treatment. The book, as a whole, represents the author's personal views, and from this standpoint is to be commended. There is little doubt, however, that he attributes to onanism an etiological importance which is unwarranted, and spermatorrhea so frequent in his experience is seldom encountered in the experience of others. There is also no foundation for the belief that sexual continence is followed by a decadence in bodily health or virility.

A. A. U.

FATIGUE AND EFFICIENCY. A STUDY IN INDUSTRY. By JOSEPHINE GOLDMARK, Publication Secretary, National Consumer's League. Pp. 893. New York: Charities Publication Committee, 1912.

"FATIGUE and efficiency" are representative of the new effort to inquire into the conditions of modern industry and to interpret them for the people at large in the light of physiological laws. The effects of overwork is the subject of a discussion at once practical and illuminating. In her effort to treat the question of fatigue from every possible point of view, Miss Goldmark has drawn her information from a dozen sources: the laboratory, the shop, the home life of the workers themselves.

The book has two divisions: (1) A discussion of the whole subject of fatigue in its dual relation, its effect on the product and its effect on the workers. In this connection, the title of this book perhaps implies that the author lays the greater emphasis on the economic result. As a matter of fact, she does prove con-

clusively that a system compelling long hours of labor must result in a deteriorated output; yet it is evident that her primary concern is in the fact that its most far reaching and disastrous results are deteriorated human beings.

Of special interest to the physician are the chapters presenting a study of the relation of fatigue to infant mortality and race degeneration. The author's conclusions are summed up in the sentence: "When overwork unfits man or woman for normal parenthood, it is in a deep sense antiphysiological and antisocial."

In the light of the general principles relating to the results of fatigue the author presents a detailed study of a number of industries which employ women, such as the canneries, the shoe manufacturing, and the telephone service. She describes the effects of fatigue that are caused not only by too long hours, but by what she calls the "new strain in industry," induced by noise, monotony, the rigid rhythm of machinery, and abnormal speed and complexity. Aside from diseases connected with specific kinds of work, the author says that the most deplorable of all the physical evils of fatigue is that it prediposes its victims to disease in general. For this reason she urges that there be a "new medical scrutiny of modern work" centred on "fatigue as itself a danger of occupation."

(2) The second division of the book given the material contained in four briefs in defense of laws especially related to women-employing industries which were filed in various courts by Louis D. Brandeis. These briefs are gathered under the significant heading, "The World's Experience upon which Legislation Limiting the Hours of Labor for Women is Based." As the title implies, they are really a symposium of conclusions in relation to fatigue which the author has gathered from the experience of various scientists, social workers, and employers of all countries.

The work is of primary value as a practical handbook for all interested in the amelioration of industrial conditions. It is written for the average reader. With its careful tabulation of facts and simplicity of thought and expression it is intelligible alike to the physician and lawyer, to the employer and social worker: in fact, even to the workers themselves whose cause it so ably champions.

H. G.

THE MEDICAL RECORD VISITING LIST FOR 1913. New York:
William Wood & Co.

THIS convenient little record book contains pages for daily and special visits; memorandum pages and pages for cash accounts. In addition there is a certain amount of information that may be of service for quick reference which includes dosage, treatment of poisoning, artificial respiration, and such subjects.

J. H. M., JR.

AN OPERATING THEATRE IN PRIVATE PRACTICE. By C. HAMILTON WHITEFORD, M.R.C.S., L.R.C.P. Pp. 76. London: Harrison & Sons, 1912.

THE author describes the building and equipment of an economical operating plant employed by him in connection with his private practice. It is well adapted to the needs of a surgeon living in a small town without the facilities of a large general hospital. Many of the original ideas in the book could be well copied in the operating rooms of large hospitals. The lighting of the room is by a large window facing south which the author finds well suited to the English climate, being neither too hot in summer, and affording better light in winter. The fixtures are arranged as much as possible flush with the walls, thus avoiding lodgement for dust. Among interesting features noticed are, an electric heating appliance for the operating table, a simple and efficient arm retainer, and a convenient receptacle for nail brushes. Valuable points on technique from the author's personal experience are given, as to sterilization, sutures, anesthesia, preparation, and after-treatment of the patient, etc. In an appendix are found useful facts on asepsis for nurses. The work would have been more complete if illustrated by a diagram. It can be recommended to anyone contemplating building an operating room either for private or general work. R. H. I.

A MANUAL OF CLINICAL CHEMISTRY, MICROSCOPY, AND BACTERIOLOGY. By M. KLOPSTOCK and A. KOWARSKY. Pp. 371; 43 illustrations; 16 plates. New York: Rebman Company, 1912.

THIS book is a translation of a valuable laboratory manual which covers not only the technique of the common clinical laboratory examinations, but also that of some less familiar that are of use in the study of the secretions of the conjunctiva, nose, mouth and pharynx, and of the sputum, gastric contents, urine, feces, blood, puncture fluids, and skin. Throughout the book much attention is devoted to bacteriological procedures, which are, for the most part, described in detail. The value of the volume is, however, seriously impaired by the extraordinary character of the translation of some portions. In a footnote on the first page the statement occurs: "All degrees of temperature quoted in this book are Celsius." For American readers "Centigrade" should have been used instead of "Celsius." In the first chapter the German "Klatsch-preparata" is never translated to the equivalent "cover-slip preparation." One is tempted, however, to close the book on coming to such a sentence as the following: "Diphtheria bacilli decompose dextrose and levulose under acid formation,

pseudo-diphtheria bacilli, as proven in numerous types of various origin are almost always inactive in both kinds of sugar, and, but in rare cases, they are active in one, never in both." Or this: "Regarding their motility the views are divided. Some authors believe them to be immovable." Or this: "They (spirochete) are corkscrew-shaped, very motile in shape and size, however, very much different from each other." Even more serious is the error on page 7, where the statement is made that "Ox serum is rendered sterile by *discontinuing* sterilization at 55°." The correct reading is "by *discontinuous* sterilization." Fortunately no other chapter contains errors as absurd as those which render the first chapter more ludicrous than useful. The section on the Wassermann reaction is not entirely clear, being especially indefinite in that portion dealing with the titration of amboceptor and complement. On the other hand, the sections on gastric contents, feces, and urine are of great value, and include material not found in other laboratory manuals. The section devoted to the blood is brief and less complete. It is unfortunate that the value of so excellent a manual is diminished by imperfections in translation.

J. H. A.

ARTHRITIS: A STUDY OF THE INFLAMMATORY DISEASES OF JOINTS.

By PETER DANIEL, F.R.C.S., Senior Surgeon, Metropolitan Hospital; Surgeon to the Gordon Hospital; etc. Edited by JAMES CANTLIE, M.A., M.B., C.M., Aberd., F.R.C.S. Eng., Surgeon, Seamen's Hospital Society; Lecturer on Surgery, London School of Tropical Medicine. Pp. 515; 131 illustrations. New York: William Wood & Co.

WITH an apology for unorthodox views, Cantlie has edited for Daniel a volume purporting to be a "study," but in reality more nearly resembling a student's compend.

It is crowded with matter, old and new, for the most part somewhat dogmatically expressed. Daniel, however, has evidently seen and considered an amount of clinical material which justifies some individuality of opinion, and enables him at times to advance points of value.

The text is punctuated by capitals, italics, and parallel tables to a rather unfortunate degree, even though the book is designed as a "practical help." In respect to scope and breadth of purpose, it deserves a wider field.

The illustrations, which are numerous, are usually semi-diagrammatic, but sometimes so inartistically done as to offend the reader in this age of pictorial excellence.

The English is careless, frequently loose enough to obscure the meaning, and at times ungrammatical. The book is rather heavy, and the type good. It is to be regretted that this possibly useful effort must be so heavily discounted.

R. P.

A TEXT-BOOK OF HUMAN PHYSIOLOGY, INCLUDING A SECTION ON PHYSIOLOGIC APPARATUS. By ALBERT P. BRUBAKER, A.M., M.D. Fourth edition. Pp. 736; 377 illustrations and 1 colored plate. Philadelphia: P. Blakiston's Son & Co., 1912.

It is pleasing to note that this excellent text-book has met with such a well-deserved demand as to require a fourth edition. Those who have had a long experience with students can see evidence upon every page of the fact that Professor Brubaker is an excellent teacher. When presenting a problem he has mastered the art of knowing where to start. Too often authors of the text-books now generally used, assume that the student's general knowledge of anatomy, histology, physics, chemistry, and even biology is such that they are free to plunge at once into a discussion of physiological material of the most intricate sort. It is true that the preparation of the student in the fundamental subjects leading to physiology is constantly improving, nevertheless, much of the data requires a thorough knowledge of details which are not given an important position or are entirely neglected in the presentation of the fundamental subjects. In consequence, a problem sometimes cannot be understood even by a well-prepared student, because he is not sufficiently familiar with the particular data from which the investigations start. This book does not neglect such data and therefore contains more histology, etc., proportionately than is found elsewhere, but, although starting a problem from the beginning, the book is never tedious for the necessary material is very briefly stated. This is shown by the size of the book which hardly exceeds 700 pages yet contains all of the physiology required in any of the best medical schools.

This edition also shows the intimate knowledge which the author possesses of the requirements of the up-to-date student and practitioner. He gives sufficient consideration to all of the physiological problems and methods which are interesting the medical profession today. For example, he goes into the subject of venous pulse in a most satisfactory manner. Likewise the pituitary bodies and the adrenal glands are considered from a physiological standpoint in a most conservative yet thorough manner. Even the finer points such as the auscultatory method of determining blood pressure is referred to. These are, however,

only a few of the instances which convince one that the book is in every way equal to the requirements of the student and practitioner.

It is pleasing to see too that the author does not avoid what are usually considered uninteresting subjects, provided they are of practical value. The physiology of the skeleton, so important to the practitioner, is often given brief consideration or entirely omitted in many books of this size. Recognizing the inestimable value of the subject in medicine the author has devoted an entire chapter to the skeleton and it has proved one of the most valuable in the book.

E. L.

PATHOLOGY OF THE EYE. By P. H. ADAMS, M.A., M.B., D.O. Oxon., F.R.C.S., Surgeon to Oxford Eye Hospital; Consulting Ophthalmic Surgeon to the Radcliffe Infirmary. London: Oxford University Press, 1912.

THIS is an excellent little manual. It takes up in turn the different structures entering into the formation of the organ, gives a brief anatomy and then describes the appearances caused by the various disease processes as they occur in the special tissues. The introductory chapter gives a short account of the methods of embedding, mounting, staining, while the last chapter is a brief description of the bacteriology of the eye. The descriptions must necessarily be brief in a small work like the present and this is about the only criticism to be made, they are almost too brief—a criticism not directed against the author, who has succeeded very well indeed with the limited space at his disposal, but one which is inherent in the plan of the work. The book is hardly adapted to the novice who requires more detailed description but rather we presume as a sort of *vade mecum* for the reader who has some acquaintance with the subject. It need scarcely be said that the recent discussions, not to say, final results find a place; thus the Chlamydozoa in trachoma together with the method of staining are described; there is a short account of retinal arteriosclerosis, etc. We note that of the varieties of choroidal inflammation syphilis and tubercle are alone mentioned.

The book is attractively gotten up; it is convenient in size; the paper, type, and binding are all that can be desired. T. B. S.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Relation of Aortitis to Syphilis.—CUMMER and DEXTER (*Jour. Amer. Med. Assoc.*, 1912, lix, 419) demonstrated a positive Wassermann reaction in the sera of 27 cases of aortic disease in a series of 36. This is 75 per cent., and is almost identical with the larger series by Longcope (74.1 per cent. of 182 cases). Seventy and three-tenths per cent. of these were men, and Cummer and Dexter think that this suggests the possibility of the conjunction of hard labor with syphilis determining the aortic location. Most of the cases were men who had been occupied as day laborers, masons, brick-layers, etc. The average number of years since the appearance of the chancre was about seven-teen. The process is distinctly a late one, and the period of latency a long one. Cummer and Dexter emphasize the indefiniteness of symptoms—pain referred to the upper sternum, a sense of constriction, dyspnea, and dulness in the second intercostal spaces extending to the left and right of the manubrium. Alleviation of pain occurred after mercurial treatment, which is urged so long as the Wassermann reaction is positive, with the hope of arresting the process.

Prophylactic Vaccination against Epidemic Meningitis.—Encouraged by the wonderful results obtained by extensive prophylactic typhoid vaccination, SOPHIAN and BLACK (*Jour. Amer. Med. Assoc.*, 1912, lix, 527) undertook to employ similar methods of prophylaxis against epidemic meningitis in the recent Texas epidemic. They emphasize the need of prophylactic measures when it is estimated that the number of healthy carriers exceeds the sick by ten or twenty times. The vaccine consisted of a killed culture five generations old, sterilized by

heat, and standardized. Eleven students were vaccinated at seven-day intervals, with three doses of 1,000,000,000 2,000,000,000, and 2,000,000,000 bacteria respectively. A slight leukocytosis followed, with malaise, headache, and fever. Occasionally signs were present suggesting meningeal irritation—severe headache, vomiting, vertigo, and photophobia. A local reaction with redness and swelling, and adenitis is the rule. The reaction lasts twenty-four hours. The immunity acquired was measured by agglutination and complement-fixation tests. The agglutinins increased after the repeated doses, one patient developing them to a titer of 1 to 1500 dilution of the serum. The highest complement-fixation was obtained in serum dilution of 1 to 250, at the end of the third week. All evidence points to the efficacy of the injection of dead meningococcus for prophylactic vaccination, as a measure which will confer considerable immunity in most cases against the infection of epidemic meningitis. The cases will be followed to determine the persistence and duration of the immunity.

Endemic Typhus Fever (Brill's Disease).—NICOLL, KRUMWIEDE, PRATT, and BULLOWA (*Jour. Amer. Med. Assoc.*, 1912, lix, 521) report a unique instance in the history of the endemic form of typhus fever (Brill's disease), in which the disease affected four members of the same family, two parents and their children. Clinically they represent types of the disease varying from the comparatively mild to an example of typhus fever such as is commonly seen in epidemics, thus giving, as it were, a clinical demonstration of the identity of the endemic and epidemic forms. The patients were Russian Hebrews of the poorer class and all were infested with head and body lice. Inoculation of the blood of one of the patients gave positive results in two guinea-pigs whose blood, in turn, injected into a monkey, caused a typical typhus temperature reaction. The authors have shown for the first time that it is possible to infect guinea-pigs with the disease, an additional point of similarity to the epidemic type.

Treponema Mucosum and Pyorrhea Alveolaris.—NOGUCHI (*Jour. Exper. Med.*, 1912, xvi, 194) isolated a small spirocheta from the pus of a case of pyorrhea alveolaris which is characterized chiefly by its capacity to produce mucin and a strong fetid odor. It is an anaërobe, and requires the presence of serum constituents for its growth. Subcutaneously it produces an acute inflammation and the tissues remain indurated a week or ten days. But there is no tendency to suppuration. The organism is easily differentiated. It has been named *Treponema Mucosum* and Noguchi holds it at least in part responsible for the strong fetid odor in the discharge from pyorrhea alveolaris.

Experimental Bronchopneumonias.—Following the experimental production of lobar pneumonia by intrabronchial insufflation of pure cultures of pneumococcus (Lamar and Meltzer), the advisability was suggested of applying the same method to the action of organisms usually found in association with bronchopneumonia. This was done by WOLLSTEIN and MELTZER (*Jour. Exper. Med.*, 1912, xvi, 126). Cultures of the streptococcus and influenza bacillus were injected

through a tube deeply into a bronchus. With the streptococcus 19 dogs killed at intervals showed typical pneumonic lesions in various stages of progression and resolution. Compared to the mortality of 16 per cent., the bacteremia, the lobar consolidation, the frequency of pleurisy, and the importance of fibrin formation in the experimental pneumococcus pneumonias of Lamar and Meltzer, these streptococcus infections showed practically no mortality, no bacteremia, a lobular type of consolidation, no pleurisy, and an unimportant part played by fibrin. The same held true for the influenza bacillus. Wollstein and Meltzer conclude that the proper invasion of the microorganism is the determining factor in the development of pneumonia, the condition of the animal being only a minor element. Different types of pneumonia are produced by specifically different bacteria.

The Cobra Venom Hemolysis Test in Syphilis.—For about five weeks after the primary lesion in syphilis the red cells are hypersusceptible to cobra venom hemolysis in all dilutions. After this they acquire tolerance and become resistant to this hemolytic agent. In no other condition or disease does this occur. STONE and SCHOTTSTAEDT (*Arch. Int. Med.*, 1912, x, 8) have applied this test to 130 patients. The washed corpuscles are mixed with cobra venom in dilutions of 1 to 10,000, 1 to 15,000, 1 to 20,000, and 1 to 30,000. All bloods hemolyze in 1 to 10,000; all normal bloods in all dilutions; in secondary syphilis the cells resist in dilutions above 1 to 10,000. In 4 cases of primary syphilis the test was positive (resisting hemolysis) in only 1. In 22 cases of active secondary and tertiary syphilis, 20 or 90.9 per cent. were positive. Thirty-three cases of latent secondary and tertiary syphilis yielded 87.8 per cent. positive. In 20 "clinically cured" cases the reaction was uniformly negative. Compared to the Wassermann reactions, an average positive percentage of 88.5 per cent. in 4200 cases of active syphilis, the cobra venom test gives about the same results, 85.4 per cent. positive in 1279 cases. But for latent syphilis, the positives averaged 78.1 per cent., compared to only 52.1 per cent. of Wassermann positives. The cobra venom and butyric acid tests agreed in 85.4 per cent. of 13 cases. Controls were negative.

The Wassermann Reaction Post Mortem.—H. SCHMIDT (*Deutsch. med. Woch.*, 1912, xxxviii, 802) has examined the sera of 233 cadavers for the Wassermann reaction. In many instances determinations had also been made during the life of the patient, in some cases as long as six months before death. Incomplete hemolysis was designated as a positive reaction. Of 34 cases whose sera were examined both before and after death, corresponding results were found in 31. In older cadavers Schmidt finds that the serum may be examined in the active state. In this case a negative reaction is of considerable value, but if the reaction is positive, a control with inactivated serum must be made. In 94 per cent. of cases, lues in any form may be determined by examination of the serum obtained at autopsy. However, it must be remembered that in tumor cachexias, severe tuberculosis, and sepsis, the reaction may at times be positive, though the hemolysis is usually incomplete. Schmidt believes that the reaction possesses a relatively high value at autopsy.

Decreased Resistance of the Erythrocytes after Consumption of Alcoholic Drinks.—F. v. FILLINGER (*Deutsch. med. Woch.*, 1912, xxxviii, 999) has repeated and confirmed v. Liebermann's observations upon the lowering of the resistance of the erythrocytes after drinking alcohol. His observations were made on man and animals. The technique he employed is the same as that described by v. Liebermann. Only a few observations are reported, but they appear to show that alcoholic drinks produce a marked, rapidly developing decrease of the erythrocytes to hypotonic salt solution in persons whose bodily resistance is already somewhat below par. The phenomenon is of short duration. Measurement of the resistance of the red cells to 0.5 per cent. salt solution is thus not only a means of determining the resistance of the individual, Fillinger contends, but it is also a convenient method of determining directly injury to the organism by alcohol and of following the extent of the injurious effect. It is desirable that similar observations be made on chronic alcoholics.

The Diagnosis of Internal Injuries Affecting the Pancreas.—J. WOHLGEMUTH and Y. NOGUCHI (*Berlin. klin. Woch.*, 1912, xlix, 1069) call attention to the difficulty of diagnosing injuries to the pancreas as a result of severe trauma of the abdominal wall. At present, there are only two methods of procedure—exploratory laparotomy and observation of the patient for a variable time. It is, therefore, desirable to have some means of ascertaining pancreatic injuries within a few hours after the traumatism has occurred. Wohlgemuth has shown that lacerations of the dog's pancreas give rise to a rapid and marked increase in the quantity of diastase in both blood and urine. The method he employed required twenty-four hours for its completion, which is a great disadvantage in the study of human cases, and he has, therefore, so modified it that the result may be obtained in one-half hour. The method is as follows: 4 to 5 c.c. of blood are defibrinated and centrifugalized at once to obtain the serum. A series of ten test tubes, numbered, is then prepared and filled with serum. Tube No. 1 contains 1 c.c. of serum, No. 2 contains 0.5 c.c., and so on, to tube No. 10, which contains 0.002 c.c. of serum. The quantity of serum added is thus one-half the quantity placed in the preceding tube of the series. To each of the test tubes now add 2 c.c. of 0.1 per cent. starch solution (Kahlbaum's soluble starch) and place all the tubes in a water bath at 38° to 40° C. for thirty minutes. Remove the tubes, cool them quickly, and then add fiftieth normal iodine solution a drop at a time. The tube in which the first bluish tint appears, is noted. It is then evident that the next preceding tube in the series, which showed no blue color, contained sufficient diastase to convert all of the starch into dextrin. Knowing the quantity of serum in this tube, which has converted 2 c.c. of starch solution to dextrin, the amount of starch solution, which 1 c.c. of serum would convert, is calculated. The result is expressed thus, $d_{\frac{3.8}{10}}^{\circ} = 32$, for example. Using this method with normal human sera (150 cases) Wohlgemuth and Noguchi found the normal value to be 8 to 16; the highest normal value found was 32. Thus, if a lesion of the pancreas is suspected in a patient who has received a severe blow on the abdomen, a value of 64 greatly strengthens the supposition. The diagnosis

is practically certain if the quantity of diastase rises. The examinations must be begun soon after the injury. Beyond seventy-two, or, at the most, ninety-six hours, the diastase will probably have returned to normal. The increase is attributed to escape of pancreatic juice into the peritoneal cavity, with subsequent absorption into the blood. Since the increase of blood diastase leads to increase of the urinary diastase, the urine should also be examined for confirmatory evidence. Normally, in the urine of man $d_{36}^{38.0} = 16$ to 32; it never exceeds 64. In 2 human cases Noguchi has used this method with success. The work will be reported by him in detail in the *Archiv f. klin. Chirurgie*.

Fatty Stools in Basedow's Disease.—A. BITTORF (*Deutsch. med. Woch.*, 1912, xxxviii, 1034) reports a case of severe exophthalmic goitre, in which fatty stools were observed. Falta reported 6 similar cases in 1910 and assumed that the condition was due to a disturbance of the internal secretion of the pancreas, though in his cases the external secretion was apparently not examined. In the present case, Bittorf has shown that there was an insufficiency of the external secretion. There was almost a total absence of trypsin and an excess of unaltered muscle fibers in the feces. After the administration of pancreon, the fat content of the dried feces sank from 50 per cent. to about 17 per cent., the fat loss in percentage of fat intake from 60 to 75 per cent. to 14 to 15 per cent. Alimentary glycosuria could not be tested in this case, but Bittorf has frequently observed it in Basedow's disease, and believes that there is no relation between fat and carbohydrate derangements in this disease.

The Treatment of Rat-bite Disease with Salvarsan.—S. HATA (*Munch. med. Woch.*, 1912, lix, 354) has collected the data of 8 cases of rat-bite disease, occurring in various parts of Japan, all of which were treated with salvarsan. The salvarsan was administered at different stages of the disease and also in the febrile and afebrile periods. In all instances the injection of salvarsan produces a striking result. Except in 3 cases, a single intravenous injection sufficed to prevent further manifestations of the disease. There was observed, however, a rise of temperature in the night following the injection or several days later, but none of the other characteristic symptoms of the paroxysm was present. Hata interprets this elevation of temperature as a reaction from the drug. With defervescence there was a marked and rapid improvement of the general condition of the patient, the inflammatory processes disappeared, and the exanthem cleared up. Gradually the tumefaction of the lymphatic glands went down, and within a few weeks the patients were well. In 1 case, however, a cure was not obtained, though there was great improvement. In 2 cases recurrences were met with, but the dose of the drug employed was too small. Hata is unwilling to say that salvarsan is a specific in rat-bite disease, but the results are better than those obtained with other forms of treatment.

The Differentiation of Human and Bovine Tubercle Bacilli by Cutaneous Infection of Guinea-pigs.—E. TOMARKIN and S. PESCHIC (*Deutsch. med. Woch.*, 1912, xxxviii, 1032), at the suggestion of Prof.

Kolle, have undertaken to determine whether human and bovine strains of tubercle bacilli may be differentiated by their varying virulence to guinea-pigs. The procedure they have employed consists in shaving the skin of the abdomen and then rubbing a measured quantity of the infectious material into the skin for two to three minutes, using a glass rod. With ordinary care the skin may be shaved so that there are no abrasions visible on inspection with a hand lens. The material they used for inoculation was obtained from various sources, that is, human tuberculous cultures, sputa, urine, and cavity contents, and bovine tuberculous cultures and glands. Tomarkin and Peschic found that the great majority of animals inoculated with human material remained healthy (of 52 guinea-pigs only 7 developed tuberculosis), whereas all animals inoculated with bovine material—whether cultures or diseased tissues—developed tuberculosis of the regional lymphatic glands and, later, generalized tuberculosis (26 guinea-pigs in all). They noted further that in none of the animals did local signs develop at the site of inoculation. Whenever infection occurred, the regional lymphatic glands were first enlarged. This striking difference in infectivity Tomarkin and Peschic attribute to variation in virulence of the two types for the guinea-pig. The study is being continued.

SURGERY

UNDER THE CHARGE OF

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The Reinforcement of the Pelvic Suture in a Pyelolithotomy by a Pedunculated Flap from the Fibrous Capsule of the Kidney.—PAYR (*Zentralbl. f. Chir.*, 1912, xxxix, 1505) for several years has been restricting the operation of nephrolithotomy in favor of pyelolithotomy. It is becoming established that it is best to adapt the operation to the individual case rather than to employ one method for all cases. Factors which will determine the operation to be done are: The situation, size, and number of the stones present; the topography and size of the pelvis of the kidney, since in some cases inflammatory changes about the kidney prevent its being delivered; the presence or absence of an infection of the calculus kidney; and whether a unilateral or bilateral lithotomy is necessary. The objections to a nephrotomy are, chiefly, the anatomical and functional damage done to the organ, and a dangerous hemorrhage which may call for a nephrectomy. The chief objec-

tion to a pyelolithotomy is that, occasionally, the wound in the pelvis gives rise to a chronic fistula. A second objection is that the exposure and removal of the stone embedded in the calyces and parenchyma of the kidney are faulty. These difficulties, however, are experienced with a nephrotomy. After the latter operation, extensive infarction and necrosis may occur with considerable reduction in the functional value of the organ. In the greater number of pyelolithotomies, smooth healing occurs. It is very likely that in the earlier cases an overlooked stone in the lower segment of the ureter, was responsible for the persistency of the fistula. Strictures and kinking of the ureter favor it also. When a pyelolithotomy is done for the removal of the stone, in approximately aseptic cases, the wound in the pelvis should be closed immediately with an exact as possible continuous suture. This necessitates a certain degree of mobility of the kidney, so that it can be brought into the wound. It is frequently recommended to suture the pelvic wound in two layers, and to cover the wound by suturing over it the surrounding fatty and fibrous tissue. But under normal conditions the material is not suitable for such a procedure, while in the presence of inflammation or abscess, it will be much worse. In several cases Payr has employed a flap of the fibrous capsule of the kidney to cover over and reinforce the suture of the wound in the pelvis. In one case there were one large and several small renal calculi in the right kidney. The urine was purulent, and the right ureter was inactive, chromocystoscopically. The walnut-sized stone was delivered with some difficulty, and a projection on it produced a small perforation in the very weak pelvic wall, to one side of the longitudinal incision. After the removal of the remaining calculi and cleansing of the cavity, the incision was sutured in a double layer (catgut and silk), and the sclerotic and irregular fatty tissue was brought over the lateral perforation. A large right-angled flap of the fibrous capsule, of two finger's breadth, with its pedicle at the hilum, was lifted and turned over on the pelvis, and beginning of the ureter. It was made to apply itself around them, and was fixed in position by a number of fine cat-gut sutures. Notwithstanding the unfavorable inflammatory conditions for making the closure water-tight, healing occurred without leakage and without reaction. The patient left the hospital in twenty-one days.

The Principles Underlying the Surgical Treatment of Gastro-intestinal Stasis, Due to Causes other than Stricture or Ulcerative Conditions.—COFFEY (*Surg., Gynec., and Obst.*, 1912, xv, 365) presents an exhaustive study of this condition. He says that there is a direct relation between gastro-intestinal stasis and abdominal ptosis, which is purely physical and mechanical. Mechanical obstructions always occur at the point of junction of a fixed and movable part of the intestinal tube, except when due to inflammatory adhesions. In 20 per cent. of human beings the ascending and descending colon have a mesentery like that of the quadruped, except at the flexures where the colon is usually attached to the front surface of the kidneys. In these defective persons the colon, instead of resting on a shelf or decline above the psoas muscle, is suspended by a direct drop from the kidney. All cases of floating kidney, mobile cecum, and general

visceroptosis, are found in this defective one-fifth of the human race. Midline ptosis produces stasis only when the normally fixed points at the second portion of the duodenum, or at the hepatic or splenic flexures, or both, remain fixed. Therefore, midline ptosis producing stasis, not only is no part of a general ptosis, but cannot exist with a general ptosis. As a rule, it is independent of any other form of localized ptosis. It is an acquired condition resulting from the combined effects of a chronically loaded colon or an overdistended stomach plus long-continued or severe exercise, or occupations requiring long standing, which stretches the normal supports. General visceroptosis is probably impossible in normal individuals having perfect fusion of the ascending and descending colon with the parietal peritoneum, which explains the fact that the great majority of individuals will not develop ptosis, no matter how thin they become nor how flabby their abdominal muscles become. The large majority of ptoses may be successfully treated, and the patients made comfortable by medical and dietary measures. Surgery should never be considered for the treatment of ptosis *per se*. Given a case of right-sided ptosis with a moderately movable right kidney, painful cecum and appendix, not relieved by medical measures, the proper treatment is removal of the appendix and fixing the ascending colon through a right rectus incision, plus fattening. This will be sufficient to retain the kidney in position. If the right kidney is exceedingly movable, and the symptoms demand surgical relief, the appendix is removed and the colon and kidney both fixed through a posterior incision. A coexisting pericolic membrane may or may not be removed, according to the judgment of the operator at the time. Usually Coffey has not removed it. An operation which fixes a floating kidney without fixing the colon at the same time is not a sound surgical procedure. A mobile cecum, with or without the membrane in which the hepatic flexure remains fixed is best treated by fixing the cecum and ascending colon to the parietal peritoneum. Midline ptosis of long standing not relieved by proper medical treatment, is successfully treated surgically by shortening the ligaments of the liver and stomach, suturing the omentum to the abdominal wall, and expanding the upper abdomen. The results following this method of treating midline ptosis with stasis are fully as striking and complete as those produced by a gastro-enterostomy for mechanical obstruction at the pylorus. Sigmoid ptosis, producing severe stasis, can only be treated successfully by short circuiting or excising. General visceroptosis, the pathognomonic sign of which is a floating left kidney, is not a surgical condition. Such patients may be materially benefited and made very comfortable by wise medical treatment combined with Martin's gymnastic treatment, but they can never be made normal individuals. The only hope for successful surgical treatment of general ptosis must be in the line of a prophylactic or orthopedic operation, which may be made possible in the future by improved diagnostic technique which will enable the doctor to determine the cases of movable colon in the feeble child before the ptosis habit has been formed; in which case the defect may be remedied by fusing the ascending colon to the parietal peritoneum, just as we now repair a congenital hernia or a cleft palate. In all of his early work, including the very first case of the surgical treatment of ptosis,

Coffey has kept his patients on the back in the Trendelenburg position for at least four weeks after operation, using practically the same position as has been recently so well described by Franklin H. Martin. Coffey concedes that in bringing forward this subject of stasis and ptosis there is being opened up one of the most dangerous fields for surgical abuses that has ever been opened to the surgical "confidence" man, who needs no other excuse for performing a surgical operation than the consent of the patient. X-ray observation, while of inestimable value in the study of these cases, is the most dangerous agent yet placed at the disposal of the unscrupulous surgeon, because it is so convincing to the laity, and at the same time so meaningless when considered independently of the history of the case, and not properly interpreted.

External Anthrax in Man.—HEINEMANN (*Deutsch. Zeitsch. f. Chir.*, 1912, cxix, 309), after a critical study of the various methods of treatment, based upon his own material and statistics of 2000 cases, says that conservative and operative methods of treating anthrax are both rational, although, according to theory and practice, the operative is the better method. The operation must consist in a radical destruction of the carbuncle. The local therapy is to be combined with serum, salvarsan, and collargol therapy, when general infection threatens or is present. The statements concerning the damage done by the operation, are to be ignored. Only an incomplete operation can do damage. A complete operation can only do good.

The Treatment of Fistula in Ano.—ELTING (*Annals of Surgery*, 1912, lvi, 744) for a number of years has been trying to perfect a method of operating on this condition which would at the same time insure healing of the fistula within a reasonably short time, and leave the patient with as nearly a normal rectum as possible. He has made a careful study of more than 100 consecutive cases of fistula in ano. He finds that probably not more than 10 per cent. of fistula in ano are tuberculous, and that a great majority of these are secondary to demonstrable lesions elsewhere in the body, usually in the lungs. The great majority of fistulae in ano originate from a diseased condition of the rectum, existing in the lower one and one-half inches, and that the diseased condition is usually a hemorrhoid. The operation which he performs is done as follows: He first dilates the rectal sphincters, laterally, as this has been shown to produce less disturbance of the bladder function than when done anteroposteriorly. With a probe the general course of the sinuses is located, and the communication with the bowel determined, if one is demonstrable. A circular incision at the junction of the skin and mucous membrane is made, and the bowel dissected away from the external and, if necessary, internal sphincters, which are carefully pushed upward and away from all possibility of injury. The dissection of the bowel is continued upward until well above the level of the internal opening, if one exists, or to the attachment of the levator ani muscle if no internal opening can be demonstrated, care being taken to keep as near the mucosa as possible. In this way complete separation of the fistulous tracts from all communication with the bowel is effected. The external fistulous opening or openings are then somewhat enlarged, and with a small curette all

the demonstrable fistulous tracts are carefully curetted. Counter openings in the skin are made in tortuous complicated fistulous tracts if necessary. With interrupted silk sutures, the bowel, mobilized and cut off above the level of the internal fistulous opening, is approximated to the skin at the anal margin, the sutures being placed in such a way as to obliterate all dead space. The fistulous openings are lightly packed with gauze, and a rectal plug is inserted for a few hours to control oozing and insure approximation of tissues, and the operation is completed. The fistulous openings are kept open with gauze for a few days and then allowed to take care of themselves, no particular treatment being required after the first week or ten days. The bowels are moved with a mild cathartic at the end of forty-eight hours, the silk sutures come away of their own accord. Of the 105 consecutive operated cases upon which this report is based, in practically all in which it has been possible to trace the subsequent history of the patients, and in all of them, so far as Elting has been able to determine, the fistulæ have healed and remained well.

A Plastic Operation on the Dura Mater by Using the Fascia Lata for Grafting Material.—MAUCLAIRE (*Archiv. gén. d. Chir.* 1912, vi, 1, 1172) reports a case of a gun shot wound of the right fronto-temporal region in which the ball lodged itself near the occipital bone, a little to the left. A trephine opening was made and this was enlarged a little by forceps. Several attempts to feel the ball by an exploratory needle failed. After a second x-ray was taken a second operation was done eight days after the first, when the ball was easily and rapidly removed. But in the two operations the dura mater had been much lacerated, and it was found impossible to suture its margins together. A fragment of the fascia lata, 4 cm. long and 4 cm. wide, was removed with a little of the muscle attached, and laid over the breach in the dura mater, between it and the bone. Then the button of bone removed by the trephine was reapplied over the whole. No drainage was employed. Healing was regular and no abnormal prominence resulted.

Concerning the Value and Character of the Cammidge Reaction in Pancreatic Diseases.—MAYESIMA (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxv, 403) says that the diagnosis of pancreatic diseases in life is often very difficult and in many cases is almost impossible. He concludes that the Cammidge reaction possesses no diagnostic importance in pancreatic diseases. The crystals which he obtained in his examinations were not always of the same chemico-physical character. Consequently the basic substance for the osazon crystals cannot be uniformly the same. The melting point and the estimated contained crystals show that the normal acids of the urine will cause a failure of the Cammidge reaction in most cases. From the treatment of the urine with the tribasic acetate of lead, according to Cammidge's advice, the glukoron acid cannot be completely removed. The Cammidge body is neither phenylhydrozin combined with lead, nor glukosazon, as maintained by Ham and Cleland, and Sehum and Hegler. In the formation of the crystals, pentosane may precipitate, as Cammidge said, as well as other little known carbohydrates.

An Experimental Contribution on the Formation of Venous Capillaries in the Kidney.—ISOBE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxv, 415), in a previous paper, studied the formation of the arterial capillaries in the kidney after implanting a portion of the omentum in a wound made in the kidney, or after surrounding a decapsulated kidney with omentum. In the venous experiments, which were done chiefly on rabbits, after a variable period following the attachment of the omentum to the kidney, the renal vein of that kidney was divided between double ligatures close to its entrance into the inferior cava, and finally the opposite kidney was extirpated. After the death of the animal the vessels were studied chiefly from the effects of venous stasis. The normal collateral venous capillaries are too scanty, at least in rabbits, to permit a compensation for the stasis in the kidney produced by ligature of the renal vein and a re-establishment of the circulation. Not one of the animals survived extirpation of one kidney with ligation of the vein of the other kidney and attachment of omentum to it after decapsulation. When the decapsulated kidney was surrounded by omentum, the venous capillaries became more distinct than in the normal, so that the intense stasis of the cortical substance is quickly compensated for and the renal elements return to their normal condition in a short time, even when the medullary substance is mostly degenerated. In favorable cases, in which the collateral vessels are very well developed, complete restitution may follow, so that the animal tolerates well the extirpation of the opposite kidney. After implantation of the omentum into the nephrotomized kidney, the collateral venous anastomoses between the omentum and kidney are produced incomparably more quickly and abundantly than after decapsulation and surrounding the kidney with omentum. Thus not only the cortical substance but the medullary, fifteen days after the ligature of the renal vein, show their normal characteristics and the animal, notwithstanding the short time between the first and second operations or between the second and third operations, tolerates easily the extirpation of the other kidney. This cannot be said of the animal in which the kidney has been decapsulated and surrounded by omentum. In Isobe's opinion, the decapsulation and the surrounding of the kidney with omentum, still more the implantation of the omentum into the nephrotomized kidney, is a more effective operation for ascites than the Talma-Drummond operation, because the venous collateral anastomosis in the latter, between the omentum and the peritoneum poor in vessels, will not produce as good results as that between the omentum and the kidney which is very rich in vessels. A short time before a colleague employed the method and obtained a very considerable diuretic effect.

The Treatment of Gastropotosis by a Wedge-shaped Resection of the Pars Media of the Stomach.—SCHLESINGER (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxv, 527) says that operation for gastropotosis today is frequently not undertaken because the condition is looked upon only as a part of a general enteroptosis and because the correction of it alone can accomplish little. Further, the usually employed artificial elevation of the stomach does not remove the conditions accompanying ptosis, especially not the dilatation and atony, and finally

the actual good results from the known operative methods are minimal and of short duration. He objects to the Rovsing operation particularly because of the adhesions between the stomach and anterior abdominal wall, which cause pain and interference of function. His objection to the Beyer operation, which elevates the stomach by shortening of the gastro-hepatic omentum, because of the failure of the thin, friable lesser omentum to hold the sutures, and the tendency of the shortened omentum to stretch again under the weight of the stomach. He excised a portion of the pars media with the purpose of bringing the stomach back to its normal size and shape. He says that among the gastropnoeses are a small number of advanced cases, which resist all internal therapy. When careful clinical observations show that the essential symptoms are actually gastric and are not due to the general asthenia, and when the disturbances are very severe and are not relieved after years of continuous internal therapy, then operative treatment is indicated. The operation proposed by Schlesinger is particularly indicated, because it gives rise to no adhesions. The wedge-shaped resection of the pars media of the stomach, which is most affected by the atony and is therefore functionally the weakest, accomplishes the purpose best, and removes about a third of the stomach. By the removal of this almost inactive portion, the emptying of the stomach will be much improved and the pressure on the transverse colon, which is the chief cause of the obstinate constipation, will be removed. The stomach itself will be restored to almost its normal working condition, and simultaneously the other abdominal organs which suffer from the unusual displacement of the stomach or from the traction on it, will be brought into more favorable relations. By observing the proper indications complete removal of the gastric disturbances is possible without causing other disadvantages.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Leukemia and Pseudoleukemia with X-rays.—STENGEL and PANCOAST (*Jour. Amer. Med. Assoc.*, 1912, lix, 1166) have observed the effect of x-ray treatment on over 40 cases of leukemia. The first 2 of these were treated throughout by the older method of directing the applications mainly or entirely to the enlarged spleen, before the adoption of the present technique. The results were the usual unsatisfactory and disappointing ones. In the other cases the present technique, that of directing the radiation primarily to the bones, has been employed throughout, with a few exceptions.

They have no doubt as to the superiority of the results derived by the method now employed. In a few instances it has been possible to compare the results of both in connection with the same cases in which splenic radiation was instituted with either little or no benefit, or the patient made worse; but following the change to bone radiation, a decided improvement soon became manifest. They do not believe that leukemia can be permanently cured by radiation, but they do believe that the x-ray will do more toward prolonging life during a period of comparative comfort than any other therapeutic agent yet employed. They emphasize certain features of the general technique that has been previously described in detail. (1) The application should be made systematically to the bones of the entire body, with the exception of the head, the body being mapped into definite areas for this purpose. (2) Exactness in dosage is always most important. It should be so regulated as to produce the necessary effect without inducing toxemia, if possible. (3) The frequency of the applications is equally as important. They should be made daily when possible, and prolonged periods of rest should not be permitted. (4) Direct exposure of the spleen and other secondary enlargements should be carefully avoided during the earlier part of the treatment; this applies especially to the very large spleens of the myelogenous form of the disease. (5) Applications should not be discontinued or lessened in frequency until normal conditions prevail, or as near normal as possible. (6) The leukocyte count and especially the differential count are the most important guides for continuing or stopping the treatment. (7) Arsenic is frequently a valuable adjunct to radiation, and should be used when there is a decided anemia or when the leukocyte count remains stationary for sometime at a comparatively high figure. (8) All precaution should be taken to avoid an x-ray dermatitis. (9) Radiation is contraindicated in practically all cases of acute leukemia, as it will only hasten death. In acute exacerbations of chronic cases the dosage should be much reduced, and the applications should be limited to the extremities until there are some definite signs of improvement. With reference to pseudoleukemia, Stengel and Pancoast state that in a small percentage of cases in which the enlargements are localized, apparent cures result from the x-ray treatment. The majority of cases improve under radiation, and they believe that constant treatment often will keep these patients alive and comparatively well for years. Another small group of cases do not respond at all to the treatment, and some of these may even be rendered so toxic as to necessitate its discontinuance.

Vegetable Days in Treatment of Diabetes, Gout, and Obesity.—DISQUE (*Therapie d. Gegenwart*, 1912, liii, 477) advocates a restriction of the diet to vegetables once or twice a week in patients whose diets cannot be constantly controlled. These vegetable days are useful not only in diabetes and obesity, but also in gout. When ordered for gout, purin-free vegetables and fruit must be specified; spinach, peas, and beans are rich in purins. The restriction of the diet to vegetables amounts practically to starvation, but the patients do not suffer from hunger on a liberal vegetable diet. Two such vegetable days a week will reduce the number of calories considerably, with a minimum amount of discomfort to the patient.

A Case of Obstinate Hemorrhagic Diathesis Cured by Injections of Defibrinated Blood.—RUBIN (*Münch. med. Woch.*, 1912, lix, 2171) reports the case of a woman, aged fifty years, with marked hemorrhages and extravasations of blood from both skin and mucous membranes. The patient's general condition was growing rapidly worse when Rubin injected 40 c.c. of defibrinated blood. The hemorrhages stopped the same day, and since then there has been no further manifestation of the trouble. She was given two subsequent injections of 40 c.c. of defibrinated blood to ensure against a relapse. This patient had previously been treated by the usual measures applied in hemorrhage such as calcium chloride, gelatin by mouth, and by subcutaneous injections, local styptics, etc., without the least influence on the bleeding. The rapidity with which the extravasations of blood disappeared was very striking. Marked metrorrhagia for a period of five months was a prominent symptom in this case, and the author suggests that this method may be valuable in the treatment of gynecological affections accompanied by hemorrhage.

Favorable Action of Salvarsan in Tabes Dorsalis.—LEREDDE (*Münch. med. Woch.*, 1912, lix, 2040 and 2112) believes that salvarsan exerts a most favorable action upon the course of tabes. He believes that there is no doubt that it prevents the progression of the disease and, furthermore, that it can cause the retrogression of certain lesions in the spinal roots or in the cord itself. Leredde has observed for two and one-half years a series of patients with tabes that were treated with salvarsan. A few patients were completely cured by the remedy, and in the majority of the cases the most marked symptoms have almost entirely disappeared or have become greatly improved. Leredde advises giving salvarsan in doses of 0.01 gram or neosalvarsan in doses of 0.015 gram per kilo of body weight. The treatment must be persisted in until the patient presents absolutely no symptomatic evidence of an active syphilis and until the positive Wassermann reaction entirely disappears.

The Excretion of Formaldehyde by the Kidneys of Patients Taking Hexamethylenamin.—L'ESPERANCE and CABOT (*Boston Med. and Surg. Jour.*, 1912, cxvii, 577) have applied Burnam's test for formaldehyde to the urine of over 250 patients taking hexamethylenamin, and their results are largely confirmatory of Burnam's findings. They believe that formaldehyde, to be of value as a urinary antiseptic, must be present in a concentration of 1 to 5000 or 6000. The results of 250 urines were that 130, or 52 per cent., showed the presence of formaldehyde. The reaction of the urine was of no importance. Some alkaline urines gave marked reactions for formaldehyde. Alkalies taken with or in combination with hexamethylenamin have no effect either in retarding or in hastening the excretion of formaldehyde. The duration of excretion of formaldehyde after a single dose of hexamethylenamin is from four to six hours, and therefore the remedy should be repeated at these intervals to secure the constant presence of formaldehyde in the urine. An increase of dosage does not affect the excretion of formaldehyde in negative urines. Patients not excreting formaldehyde do not have untoward symptoms, either bladder or

renal, regardless of the amount of hexamethylenamin taken. The chief conclusion to be drawn from the observations as related is that the urine of all patients taking hexamethylenamin should be tested for formaldehyde, and if not present, the drug should be discontinued as useless.

Experimental Pneumococcic Meningitis and its Specific Treatment.—LAMAR (*Jour. Exper. Med.*, 1912, xvi, 581) found that virulent pneumococci injected into the cranial or spinal cavities of monkeys produce constantly a meningitis closely resembling pneumococcus meningitis in man, except that the experimental disease pursues a more rapid course to the invariable death of the untreated animal. An homologous immune pneumococcus serum injected into the spinal canal exerts a restraining influence upon the disease to the extent that when employed early it prevented, exceptionally, the occurrence of infection, and thus saved the life of the animal and when given later it at first retarded the disease, but subsequently exerted no beneficial action, and was powerless to save life. A mixture of sodium oleate, immunal serum, and boric acid exerted regularly a more powerful action than immunal serum alone, and not only prevented the occurrence of infection, but also, when administered repeatedly, arrested the progress of an actually established infection, and led, often, to the enduring and perfect recovery of the inoculated animal. It is proposed to employ a similar mixture in the direct treatment of pneumococcic meningitis, and possibly of still other accessible local pneumococcal infections in man, because an anti-pneumococcus serum is at best active only against the homologous organisms or organisms the types of which have been employed in its preparation. Under the best experimental conditions the extent of its efficiency is confined within a brief space of time; therefore, the outlook for its successful employment alone in spontaneous disease is not encouraging.

An Experimental Investigation of the Value of Hexamethylenamin and Allied Compounds.—BURNAM (*Arch. Int. Med.*, 1912, x, 324) believes that the efficacy of hexamethylenamin and allied compounds as a urinary antiseptic is probably dependent upon their decomposition and the liberation of free formaldehyde in the urine. He describes a simple test for formaldehyde that may be applied to various body fluids. The test is delicate, down to 1 to 150,000 or less, and the amount of formaldehyde may be roughly estimated qualitatively. Former tests have not differentiated between hexamethylenamin and free formaldehyde. Experiments related by Burnam showed that hexamethylenamin solutions had no bactericidal effects, but that solutions of formaldehyde up to 1 to 20,000 had distinct bactericidal properties. A solution of 1 to 5000 formaldehyde destroyed the typhoid bacillus and the streptococcus within twenty-four hours. The clinical results obtained have conformed in every way with the assumption that it is the free formaldehyde which is the effective agent, and that it must be present in fairly strong solution. In not a single case has there been observed the slightest improvement from giving hexamethylenamin when the urine showed hexamethylenamin, but not free formaldehyde. Burnam found that in some patients it

was possible to secure concentrations of from 1 to 5000 of formaldehyde, and was stronger in the urine after the administration of hexamethylenamin. An important finding was that on the customary doses, of from 5 to 10 grains, given three times a day, not more than 2 patients out of 10 showed any decomposition of the drug into formaldehyde. He states further that, while not more than 10 per cent. of those examined showed the formaldehyde present after the smaller doses, at least 60 per cent. showed it when the dosage was made from 20 to 30 grains, repeated every four to six hours. In a few instances in which the formaldehyde was not present after dosage of 30 grains, the quantity was raised to as high as 100 grains at a single dose without causing a decomposition of the hexamethylenamin. The only toxic effect due to hexamethylenamin is occasioned by the liberation of free formaldehyde in the urine, and when this does not occur, it is safe to push the dose until it does appear. The proper treatment is to give a dose just large enough to be under that necessary to cause bladder irritation. Burnam says that examinations of the bile, sputum, saliva, and cerebrospinal fluid shows that even after rather large doses of hexamethylenamin, there appears in them but traces of the drug, certainly in percentages less than 1 to 150,000. Whether this trace is of hexamethylenamin, as seems most likely, or of formaldehyde, it is impossible to state, because the only test which would show it is Hehner's, which does not differentiate these two substances. So far as any therapeutic value is concerned, it does not make any difference because, as already shown, solutions of formaldehyde of the weakness indicated, do not possess any antiseptic value. Burnam believes, therefore, that the use of hexamethylenamin for the curing or bettering of, or as a prophylactic against infections of the bile passages, respiratory passages, and cerebrospinal system is illusory, and cannot possibly yield results. He has no explanation to offer for the reported clinical and bacteriological improvements, for, with the exception of the urine, he has not tested this side of the question. In the urine the clinical and bacteriological findings indicate that only those patients who show free formaldehyde have been improved by the drug. The phenylhydrazin-nitroprusside test is simple, and when applied gives the physician an easy method of determining the dose of hexamethylenamin which he should use, and also shows those cases in which no results from this drug can be expected. The test is of value in determining the efficiency of compounds whose value rests on the liberation of free formaldehyde, and it is to be hoped that an endeavor will be successful in securing a substance which, when taken by the mouth, will be excreted through the kidneys and will liberate formaldehyde in the urine in every case. Although it has its limitations, Burnam's experiences show that hexamethylenamin, when properly given, in more than half the cases of urinary infection is of immense value, and at the present time superior to any other drug in common use.

The Treatment of Epilepsy by a Diet Low in Salt.—ULRICH (*Münch. med. Woch.*, 1912, lix, 1947, 2007) reports in detail the results of treating 15 cases of epilepsy by a diet low in salt in combination with the bromide treatment. He has observed these patients con-

tinuously for a period of five years, and the improvement has been constantly maintained. He noticed immediate improvement upon the withdrawal of sodium chloride from the diet. In 6 cases the attacks ceased completely; in the other 9 there was marked improvement. The convulsions not only disappeared, but the mental conditions of the patients improved, and in no case was any marked mental deterioration observed which is so common in epileptics treated with bromides. The antagonism of chloride to bromide has been established by many experiments, and Ulrich's clinical observations indicate that bromide treatment of epilepsy is much more satisfactory when the salt content of the diet is reduced. Ulrich gives the details of a method to facilitate the use of a salt-poor diet and to make the diet less monotonous for the patient.

PEDIATRICS

UNDER THE CHARGE OF

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Appendicitis in Children.—ALEX. MITCHELL (*British Jour. Child. Dis.*, 1912, ix, 355) contributes a study of 40 consecutive cases of appendicitis in children, in which the condition was acute, and the disease had extended beyond the peritoneal covering of the appendix resulting in gangrene, peritonitis or pus-formation. Most writers now agree on the need of early surgical treatment in young subjects, in which class the disease is especially treacherous and fatal. In the present series the youngest case was aged fourteen months, and the oldest fourteen years. The average duration of illness was five days. Nausea and vomiting were not prominent in all cases, but abdominal tenderness and rigidity were present at some stage of every case. In about 6 per cent. of the cases a definite history of a previous attack was obtained, but a larger proportion gave the history of previous, continued "stomach-ache." In 9 cases a large, walled-off abscess was found. Three of these cases died, and 5 of the remaining 6 had secondary operations for removal of the appendix. In 5 cases the abscess was localized, but the peritoneum had to be opened to reach the abscess. One of these cases died. In the remaining 26 cases no definite adhesions walled off the appendicular area. In 18 of these cases there was a diffuse peritonitis and a gangrenous appendix in all but one. Six of these cases died. The remaining group include 8 cases which showed a gangrenous appendix, but little or no peritonitis. All these recovered. In this series of 40 cases the mortality was 25 per cent. On the other hand, in all the cases operated on over the same period of two years in the acute stage, before the infection had visibly extended beyond the peritoneum of the appendix, no life was lost. Appendicitis in children is a dangerous and deceptive condition,

as the stage of the disease is difficult to determine. Children are poor subjects for acute septic infection of the peritoneum, the appendix is often in a high position, and adhesions are not readily formed. The safest course in children is not to be too confident of one's power to estimate the exact condition of the appendix, but to make a definite diagnosis of the disease at the earliest stage of its course, so that prompt surgical treatment may avert a fatal conclusion.

Saline Solutions in Epidemic Diarrhea.—J. ROSS MACKENZIE (*British Jour. Child. Dis.*, 1912, ix, 343) investigated the efficacy of injections of normal saline solution and sea water plasma in epidemic diarrhea. In 85 per cent. of the cases the routine treatment was efficacious. This treatment consisted, briefly, of gastric lavage, starvation for twenty-four hours, elimination by castor oil, bowel irrigation with normal saline solution, and castor oil, 4 minims every four hours as an astringent. In the 15 per cent. of cases resisting this treatment, the morbid conditions were: persistent vomiting and diarrhea, profound toxemia and collapse, and anuria. The daily urinary output is an index to the severity of the toxemia. Anuria is the key to the moribund condition in epidemic diarrhea, and is caused by lowering of the general blood pressure, and that of the kidneys in particular. Mackenzie is convinced that the subcutaneous injection of sea-water plasma, normal saline solution, or sterile water shows an immediate response, not from any particular or isolated constituent of the fluid, but from an increased blood pressure. This promotes an increased secretion of urine, and the passage of a large quantity of accumulated toxins. Normal saline solution and especially hypertonic saline solution acts more permanently, but not more rapidly than sterile water. This greater permanency is probably due to the saline constituents. The comparative value of normal saline solution and sea-water plasma in this condition cannot be estimated fully. Of Mackenzie's cases resisting ordinary treatment, 12 per cent. responded to injections of sterile water or saline solutions. The immediate effects of both these fluids were increased blood pressure and disappearance of diarrhea, collapse and anuria. Normal saline solution is as efficacious, if not as permanent in effect as salt-water plasma, and has the advantage of being cheap and easily available everywhere. The earliest indications of collapse call for subcutaneous injections of saline solution.

Are the Inclusion Bodies in Leukocytes Pathognomonic of Scarlet Fever.—H. BONGARTZ (*Berlin. klin. Woch.*, 1912, xlix, 2124) reports his observations in a study of 80 cases, relative to the inclusion bodies in the leukocytes first reported by Dörlle as occurring in scarlet fever, and corroborated by Kretschmer of Strassburg and by Nicoll and Williams of New York. The inclusion bodies are small corpuscular elements within the protoplasm of the leukocytes and distinguished from the nucleus by being less intensely stained. The three forms usually seen are in shape similar to a coccus, a bacillus, and a crescent. From 1 to 6 bodies are usually found in one leukocyte. The other three observers tended to the belief that these bodies were usually found only in scarlet fever. Bongartz's observations aimed to deter-

mine whether these bodies occurred only in cases of scarlet fever, and whether they were pathognomonic of the disease. His examinations were always checked over and corroborated by two of his assistants. He examined 80 children ranging in age from five days to thirteen years. Of this number 59 were ill and 21 were in good health. In the 21 healthy children the inclusion bodies were present in 17 cases and absent in 4 cases. The bodies were found positive in 11 cases of scarlet fever, 6 cases of diphtheria, 4 cases of acute bronchitis, 3 cases of pertussis, 4 cases of tuberculosis of the bones, 4 cases of gastrointestinal catarrh, 1 case of typhoid and 3 cases of catarrhal pneumonia. In some of the preparations, especially those of pertussis and tuberculosis the bodies were found in only a few of the leukocytes, but this was the only difference noted. Bongartz therefore concludes that the inclusion bodies are found in the protoplasm of the leukocytes in children generally. That they apparently increase in number and are found in almost all the leukocytes during febrile conditions. That it is not possible to consider the inclusion bodies pathognomonic for any one disease, certainly not for scarlet fever.

Some Considerations on Infant Feeding.—F. G. CROOKSHANK (*British Jour. Child. Dis.*, 1912, ix, 31) mentions a large number of considerations affecting infant feeding, based on clinical experience. The method of inductive logic, the hypotheses based on clinical experience is preferable to the deductive plan, and the diversity of opinions in pediatrics is unfortunate. The problem of infant feeding depends on the mother's state of nutrition during pregnancy and the amount of stimulation of the maternal glands by particular substances in the diet during and preceding pregnancy. Defective suckling power is often due to a lack of "biological galactogogues." The milk of a cow fed on lush pasturage and sweet hay has more biological value than that from a cow fed on artificial fodder such as copra, etc. The peasant woman is usually chosen as a wet nurse in preference to the town-bred product, because she is efficient biologically, having lived on food which has produced her race. This suggests the importance of the biological qualities of the food of cows and other animals that supply human aliment. Practical experience shows that if the child be healthy and the cow well fed and kempt, far less modification of the milk is necessary. Wonderfully successful results have attended Dr. Langmead's plan of giving undiluted, unboiled milk with the addition of a few grains of sodium citrate. There is probably a definite correlation between artificial feeding in infancy and the functioning of the lactiferous gland in later life. Slightly diluted, unboiled cow's milk with the addition of some malted food has been of most service to Crookshank. Fresh milk can be increased in quantity from time to time until the child is taking almost undiluted fresh cow's milk. Malt helps in massing the curd, is slightly laxative, and compensates for deficiency in cream. A little Bermuda arrow-root, well boiled, and taken nearly cold is an excellent, temporary food in intestinal disorders. Veal or mutton broth thickened with arrow-root is a good substitute for milk during the hottest weeks of summer. It is better than boiled milk, if, in making the broth, the sternum and ribs of veal and mutton are first split open. A yearling, well forward with its teeth should

have food which exercises its jaws and stimulates the ptyalin and gastric juice, and should not be fed entirely on extractives such as beef tea, etc. The demineralization attendant on tuberculosis points to the value of mineral salts in food articles. One of the biological values of food, the hormonal, is very important, and mother's milk has an homologous hormonal value. Food for mother's should be least interfered with in manufacture or cooking.

OBSTETRICS

UNDER THE CHARGE OF

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Prolapse of the Placenta.—HARTMANN reports from Meyer's clinic in Copenhagen (*Monatsschr. f. Geb. und. Gyn.*, 1912, Band xxxv, Heft 5) the case of a multipara who had suffered from prolonged albuminuria following diphtheria in childhood. She was admitted to hospital about six months pregnant, with marked nephritis and edema. There had been bleeding at varying intervals. Shortly after admission the patient discharged clots with fluid blood, and examination showed the internal os covered by placenta. An elastic bag was inserted to hasten labor and check hemorrhage. The patient gradually became worse, the uterus becoming greatly distended, and edema of the genitals developing. It was impossible to deliver the bag unemptied through the cervix. On emptying and removing it, blood clots were delivered and also the placenta. On rupturing the membranes the fetus was delivered by version and extraction. The patient died, with great restlessness, dyspnea, and a pulse at first strong, then becoming weak. Autopsy showed chronic nephritis with characteristic changes in the heart and vessels. There was abundant serous fluid in the thoracic cavity, the pericardium, and peritoneum. The tissues were anemic. On examining the placenta the changes characteristic of nephritis were well developed.

The Influence of Vaginal Douches during Pregnancy upon the Normal Genital Tract.—POLANO (*Zeitschr. f. Geburts. und Gynäk.*, 1912, Band lxx, Heft 2) has made observations to ascertain the effect produced upon pregnant patients by vaginal douches. His observations were made upon patients not in labor, some of them in a normal condition, others suffering from vaginal and cervical catarrh. Various antiseptics and disinfectants were employed. He finds that one cannot accurately estimate the sterility of the birth canal by the comparative sterility of culture material used as a test. He believes that the growth of material upon agar is our most practical method of estimating the results obtained by different methods of treatment.

He finds that increased growth of bacteria upon agar is accompanied by increased formation of epithelial cells, leukocytes, and increased development of bacteria is observed by microscopic examination. None of the antiseptics employed produced much effect upon the chemical reaction of vaginal secretion or upon the growth of bacteria. The staphylococci were especially resistant. The most efficient antiseptics were alumn, alcohol, also, nitrate of silver, and alum. Less efficient, but still of practical value, were lysoform, and 0.2 per cent. iodine; while acetic acid, lysol, and lactic acid, were least efficient. Apparently those antiseptics were most useful which produced a shrinking and practical drying effect upon the bacteria. In this connection, the paper of AMERSBACH, from the Bacteriological Laboratory at Frankfurt (*Zeitschr. f. Geburts. und Gynäk.*, 1912, Band lxx, Heft 2) is of interest. He examined 40 normal pregnant patients to determine the presence of bacteria in the genital tract; 81 examinations made in these cases showed cocci, which could be positively demonstrated by staining. Of these, 48 per cent. were successfully grown in culture, produced hemolysis, and by their toxins could be identified as pyogenic staphylococci. The labor and puerperal periods of these patients were normal.

The Clinical and Bacteriological Study of Abortion.—BONDY (*Zeitschr. f. Geburts. und Gynäk.*, 1912, Band lxx, Heft 2) has made an extensive study of cases of abortion to determine the presence of bacteria. He finds that in the majority of cases, especially those having fever, that the well-recognized pathogenical varieties are present. In 62 per cent. of cases having fever streptococci were found. In all cases streptococci were present in 37 per cent. More than half of those having fever, and at least one-third of all cases of abortion, showed the presence of streptococci in the genital tract. In many of these patients, in addition, staphylococci, pneumococci, gonococci, and colon bacilli, were also present, so that in 81 per cent. of fever cases, infectious bacteria were found, and in 53 per cent. of those without fever. The colon bacilli were present in 37 per cent. of abortions, and in 72 per cent. of those having fever. It is difficult to establish the distinction of putrid abortion where only the germs of decomposition are present, and septic abortion. Germs are usually found in abortion only in the superficial layers of necrotic decidua, seldom penetrating to the deeper tissues. It is important in these cases to study, if possible, the presence and multiplication of bacteria in the blood stream. Ptoamines are now held to be of little importance in these cases, and septic cases are now thought to be invariably accompanied by the entrance of bacteria into the blood stream. His investigations give Bondy no reason to believe that we should make essential changes in our methods of treatment at present. In all cases of abortion germs may be found in the uterus, and those methods should be employed to disinfect the uterus which are least harmful. We cannot now distinguish between bacteria which are but little harmful and those which are actively pathogenic. In many cases the fate of the patient is already decided. She is infected, or not infected, before she reaches the hands of the obstetrician. There is no reason to adopt the use of the sharp curette in attempting to empty the uterus,

and whenever possible debris should be removed by the finger or a blunt instrument. In many cases the blunt curette is far more efficient cautiously used than the finger. Each case must be studied upon its own merits, and if remedies are used to promote uterine contraction, and care is taken to avoid injuring the lining membrane of the uterus, the best results will be obtained. Pituitrin seems to be efficient in many of these cases.

Surgical Treatment of Uterine Hemorrhage Complicating Pregnancy, Labor, and the Puerperal State.—At the Sixth International Congress of Obstetrics and Gynecology, Berlin, September 9, 1912, COUVELAIRE stated that the majority of French obstetricians treated placenta prævia by rupturing the membranes, the introduction of a bag within the cavity of the membranes, or version without extraction. The use of the vaginal tampon and rapid delivery through the vagina had been abandoned. In Pinard's clinic, in twenty years, in 53,000 labors, there had occurred 162 cases of placenta prævia with 10 deaths, a maternal mortality of 6.7 per cent. Champetier de Ribes reported 67 cases with 6 deaths, a maternal mortality of 8.9 per cent. Professor Bar had 153 cases with 14 deaths, a maternal mortality of 9.2 per cent. In the Lyons Maternity, 167 cases were reported with 13 deaths, a maternal mortality of 7.78 per cent. Ferré reported 35 cases, with 4 deaths, a maternal mortality of 11.4 per cent. The average mortality of all these cases was 8.2 per cent. If those cases are subtracted which are brought to the clinic in a practically hopeless condition through severe hemorrhage, the maternal mortality sinks to 4 per cent. Septic infection is the most frequent cause of death. Next to this, acute anemia, and then rupture of the uterus; three-fifths of all cases result from infection and shock. In but 1.2 per cent. of the fatal cases was hemorrhage alone the cause of death. It is believed that the blood loss itself is not sufficiently great in many cases to justify abdominal section, and French obstetricians limit themselves to the methods of treatment already described. With these methods the mortality among the children varies from 44 to 60 per cent. This arises from the fact that most of the children are premature, and born with little power of resistance. There is little inclination in France to adopt the extraperitoneal variety of section, and in cases where section is indicated the classic method is preferred. Should the necessity for removing the uterus arise, partial or total hysterectomy is indicated. In hemorrhage from the premature separation of the normally implanted placenta the maternal mortality is 20 per cent. This is a great improvement over the old statistics, which ranged from 50 to 65 per cent. These results are still most unsatisfactory, and in cases where the bleeding is sudden and profuse, hysterectomy is the only recourse. When the abdomen is opened the operator can judge whether he can save the uterus, or whether there are injuries or lesions which make its removal necessary. In cases of uteroplacental apoplexy where the uterine wall is enormously infiltrated with blood, dissecting the muscular substance and often distending the broad ligaments, the uterus must be removed. When the cervix is hard and resisting, rapid delivery by section is indicated, and most French obstetricians prefer the abdominal route. Jung, of Göttingen, has successfully practised

vaginal section in incomplete abortion complicated by hemorrhage. Should bleeding occur during labor the patient must be delivered as soon as possible. In the absence of contracted pelvis the vaginal route should be selected. Where placenta prævia is not threatening the use of the elastic bag is indicated, and in other cases vaginal Cesarean section. The use of the bag is difficult under proper precautions in private practice. He preferred vaginal Cesarean section to abdominal, and would carefully close lacerations of the cervix occurring during delivery. In rupture of the uterus abdominal section is indicated, as the results of the tampon have been unsatisfactory. He had never been obliged to extirpate the uterus because of atony, but the possibility of this complication could not be denied. Where hemorrhage developed suddenly and profusely he had obtained good results by bimanual compression of the aorta, which he considered much superior to Gauss' instrument or Momburg's bandage. Davis, of Philadelphia, described a simple method of controlling uterine hemorrhage in accidental separation after the uterus had been emptied. The gloved hand is inserted within the uterus, folded to make a fist, and the abdominal aorta compressed through the uterine wall at the brim of the pelvis. The presence of the closed hand excites uterine contraction, and such pressure may be continued for a short time to permit intravenous saline transfusion and the use of hypodermic stimulation. It should be followed by tamponing with iodoform gauze. He also reported 7 abdominal sections for placenta prævia, three of them performed upon mothers in an exhausted condition through hemorrhage. All of the mothers recovered, and 3 of the children. One patient has since borne a healthy living child in spontaneous labor. He had abandoned the vaginal tampon because it is likely to result in infection, especially when applied by the general practitioner in private houses. A fatal case occurring in the hands of an assistant in his clinic was reported as an example. In hospital practice he believed that abdominal Cesarean section for placenta prævia is the most rapid and certain method of dealing with this complication, and also with accidental separation of the normally implanted placenta and with ruptured uterus. Such cases demand hospital care at once. In private houses version without extraction is best adapted for the circumstances present. He also calls attention to the fact that the ovum attached to the lower uterine segment and cervix in placenta prævia is as truly ectopic as the ovum which develops within the Fallopian tube and Graafian follicle. If it is rational to treat the latter by surgical interference, it is equally indicated with the former. Zweifel, of Leipzig, believed that in placenta prævia the use of the elastic bag gave better results for the child, but was more difficult and more bloody than combined version. Cesarean section he would limit to cases of full term living children, the mother in an aseptic condition, and the placenta entirely covering the os. He had operated twice with excellent results. He had been interested to observe how complete and rapid was the cessation of hemorrhage when the uterus was opened. He preferred the transperitoneal method of operation. He placed little reliance upon the iodoform gauze tampon, but he had seen good results from Momburg's bandage. In desperate cases the total removal of the unopened uterus

is indicated. He exhibited two specimens showing the entire removal of the uterus in placenta prævia. In the last four years he has operated 6 times with 3 good results. The elastic bag he considered more efficient than the tampon. In 8 cases he had used the gauze saturated with a preparation of iron free from acid, with 6 good results. Mayer, of Tübingen, calls attention to the danger attending the use of Momburg's bandage. In 1 case the patient had hemorrhage from the veins in the lower uterine segment. The spermatic vessels in this patient must have been compressed. Experiments on animals show that by the use of this bandage the ureter may be compressed and also the renal arteries. The kidneys show distinct disturbance in function, and this is especially apt to happen in cases of nephroptosis. In latent pyelitis this would be dangerous. In some cases the action of the heart has been greatly embarrassed, and in some patients the removal of the bandage was followed by threatened cessation of the heart's action. Pankow, of Düsseldorf, would distinguish two varieties of placenta prævia: Primary, where the ovum embeds itself in the isthmus of the uterus, and, secondary, where the ovum was attached to the uterine body, a portion of it extending up the isthmus. Evidently the first is the more serious variety. In both, the vessels of the isthmus become greatly dilated. As these vessels are not controlled by contractions of the upper uterine segment, it is evident that the occurrence of labor does not close these enlarged vessels. The wall of the uterus at this point is often infiltrated with fetal cells which favor the occurrence of hemorrhage. The dilatation of the lower uterine segment which occurs during labor also encourages hemorrhage, and in some cases favors rupture of the uterus. From the anatomy of the situation, it follows that that method of treatment is best which empties the uterus promptly, removing the placenta without distending the cervix and isthmus. Abdominal Cesarean section in the classic variety fulfils these indications. The average mortality of mothers in placenta prævia in various clinics ranges from 5 to 10 per cent.; the children from 50 to 80 per cent. It seems irrational to operate to save the lives of children in contracted pelvis, and to neglect the children in placenta prævia. An early diagnosis of placenta prævia can usually be made, and if these cases are sent at once to hospital they should be in a clean condition for operation. In the Freiburg clinic, in 79 cases of placenta prævia, 38 were delivered by Cesarean section, with a maternal mortality of 2.5 per cent., and a fetal mortality among viable children of 2.9 per cent.

GYNECOLOGY

UNDER THE CHARGE OF

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Transvaginal Resection of Rectal Carcinoma.—CHALIER and PÉRRIN (*Rev. de Gyn.*, 1912, xix, 101) think that the vaginal route, where it

can be employed, offers all the advantages of the other methods of approach to the carcinomatous rectum, and possesses some of its own in addition. It can be carried out in an equally aseptic manner, permits of as wide a resection as the other methods, and preserves the sphincteric function. Its particular advantage is that it permits of more thoroughly exploring the extent of the cancer than any other method of attack from below, the extensive opening in the vagina and perineum offering a large field of operation, without producing as much shock as the methods involving a resection of a portion of the pelvic skeleton. While fissures and stenoses may follow this, as any other type of operation, they are certainly no more frequent in occurrence, and are equally amenable to treatment. The operation finds its indication particularly in cases of limited, non-adherent tumors, whose lower limit is at least 4 or 5 cm. above the anus, and whose upper limit does not extend above the upper end of the rectum (third sacral vertebra), although in a few instances even sigmoid tumors have been successfully resected through the vagina. The chief local contraindications are vaginal malformations, inflammatory genital affections, and marked decrease in the transverse diameter of the pelvic outlet (rachitic pelves). Chalié and Perrin's technique, which differs in some points from that described by previous writers, is very briefly, as follows: The peritoneal cavity is opened by the usual transverse colpotomy incision, posterior to the cervix. The extent, operability, etc., of the tumor is explored through this opening; then a vertical incision is carried downward from the centre of the transverse one, curving gradually to the left, and being continued over the perineum to the side of the anus as a Schuehardt paravaginal incision. The rectum and sigmoid are now carefully freed from their lateral and posterior attachments, this process being carried to a point at least 2 or 3 cm. above the upper limits of the tumor, and to a similar distance below the lower limits. The peritoneal cavity is now carefully closed by suturing the peritoneum lining the anterior wall of the pouch of Douglas to the serosa of the anterior wall of the pulled-down sigmoid as far as possible above the point at which resection is to be done. The tumor-bearing portion of the gut is now resected, beginning preferably above between two ligatures, and working downward. The portion of rectum remaining below the point of resection, attached to the sphincter, is now denuded of its mucosa, and the upper segment drawn down through it by means of forceps introduced through the anus, the mucosa of this invaginated upper segment being then sutured to the peri-anal skin surface. The operation is completed by closing the perineovaginal incision, introducing a small drain into the lower angle, and into each ischio-rectal fossa. The bowels are kept locked for eight to ten days. The chief postoperative complications to be feared are fistulæ and stenoses; the former are to be treated by suitable plastic operations, the latter by dilatation with Hegar's bougies. Chalié and Perrin report 2 cases operated upon by this method; the first died seventeen months after operation with generalized metastases (it seems probable that a liver metastasis may have been present at the time of operation). The second case had been done only seven weeks before the publication of the report; at that time she appeared cured, and has perfect sphincter control.

Diffuse Gonorrheal Peritonitis.—Notwithstanding the general acceptance of the fact that an ascending gonorrheal infection can produce a circumscribed pelvipерitonitis, opinions still differ widely as to the ability of the gonococcus, without mixed infection, to produce a *generalized* purulent peritonitis. While many authors accept this possibility as demonstrated, others—among them such prominent gynecologists as Bumm and Fromme—deny it absolutely, holding that in every such case reported the condition was due to a flooding of the abdominal cavity with pus from an old gonorrheal pyosalpinx, and that the gonococcus can produce a generalized, purulent peritonitis only when in symbiosis with other organisms. ALBRECHT (*Münch. med. Woch.*, 1912, lix, 2268) considers that this question is now in the stage of discussion through which have passed similar ones with regard to the possibility of pure gonorrheal infections of the endocardium, pericardium, joint cavities, etc., all of which have been definitely settled in the positive. Albrecht has observed 4 cases of diffuse, purulent peritonitis, which he believes were due solely to gonorrheal infection. One of these was a girl, aged eighteen years, who was sent to the hospital with the diagnosis of general peritonitis due to a ruptured appendix. At operation the peritoneal cavity was found full of creamy pus, which showed in smears large numbers of gonococci, and no other organisms. The appendix was normal; both tubes were swollen, and exuded pus from their abdominal ends. The entire serosa was acutely inflamed, and covered with small patches of fibrin. Growth was obtained after inoculation from the pus only on Pfeiffer's blood-agar, this proving to be a pure culture of gonococci. In the other 3 cases smears showed likewise gonococci alone, but cultures were not successful. One of these cases was a male, who had contracted acute gonorrhea two weeks previously; the others were young women. In all these patients the clinical symptoms were identical; the onset was sudden and stormy, suggesting peritonitis following a ruptured appendix, which was the clinical diagnosis in each instance. In all the symptoms disappeared immediately after removing the pus from the abdomen, and the patients made an uneventful recovery, the gonorrheal type of peritonitis showing a remarkably benign course, in contradistinction to those of other origin. Albrecht considers that these cases, and especially the first one, prove conclusively that a diffuse, purulent peritonitis can arise from pure gonorrheal infection without the presence of any other organisms; he thinks that immediate operation is indicated in all instances, as it is impossible definitely to diagnose gonorrheal from other much more common types of peritonitis.

Internal Secretion of the Ovary.—A recent contribution to this much discussed subject has been made by SCHICKELE (*Biochem. Zeitschr.*, 1912, xxxviii, 169), who has continued his experiments with extracts of various organs obtained by subjecting them to great pressure. His first report on these experiments was made about two years ago (*Münch. med. Woch.*, 1911, lviii, 123), and has already been reviewed in this department. His original experiments demonstrated that these "pressure-extracts" all exhibit a certain inhibitory action on the coagulation of blood, but the extracts of the uterus and ovaries exert

a very much more powerful effect than those from any other organ. He also showed that these extracts, when injected into the circulation of an animal, have a distinct depressor action on the blood pressure. In his later work he has been able to show that not only do differences in this coagulation-inhibiting action exist between different organs, but that in cases showing clinically no symptoms of excessive uterine bleeding, this inhibitory power is more pronounced in the ovarian than in the uterine extracts; the organs from individuals who had suffered from severe menorrhagia, on the other hand, show a greater activity on the part of the uterus than of the ovaries. He has noted further that extracts from the uterine mucosa are always more active than those from the muscle tissue, and that the action of fibroid tumor tissue is less intense than that of the uterus itself. The inhibitory substance, which he believes to be an antithrombin, is firmly combined with the cell-tissue, probably existing as an endocellular material of some sort. Although this substance gets into the menstrual blood in large quantities, it is not found in the circulating blood even of patients whose organs show unusually marked activity. An interesting fact that Schiekele has brought out is that the uterus and ovaries of women past the menopause do not show any greater activity than any other organ of the body. Since the same substance, having this anti-thrombotic action, is found in the ovaries, uterus, and menstrual blood, Schiekele considers it rational to assume that the ovaries are the source of its formation; that it is secreted by them into the circulating blood, but in such small quantities as to be undemonstrable, and is then stored up by the uterus, to be excreted by it at periodic intervals in the menstrual blood. The substance, which when injected into the circulation, causes dilatation of the vessels, with consequent fall in blood pressure, is also found in the menstrual blood, as well as in the uterus, tubes, and ovaries, but this likewise disappears after the menopause. He considers it probable that this also originates in the ovaries, whence it is carried to the uterus, but has not been able actually to demonstrate this. The occasional occurrence of vicarious menstruation would seem to indicate, however, that it may at times get into the general circulation in larger quantities than normal.

Menstruation in Healthy Individuals.—In order to determine, if possible, whether the occurrence of menstruation exerts any actual, objectively demonstrable effect upon the normal female organism, as has so often been asserted, SCHMOTKIN (*Arch. f. Gyn.*, 1912, xevii, 495) has carried out a rather interesting series of investigations. For three consecutive months she has kept careful records of the blood-pressure (systolic and diastolic), pulse, temperature, and muscular power of eight healthy young women aged from eighteen to twenty-five years, taking readings every other day, except during the menstrual period, when daily examinations were made. Her subjects for these tests were all maids employed about the clinic; their regular work had to be carried on therefore just as actively throughout menstruation as in the interval. As a result of these investigations, the individual findings of which are all tabulated in detail in the original article, Schmotkin says that she was unable to demonstrate any considerable variations in any of the factors considered in any of the subjects.

The premenstrual rise and menstrual fall in the curve representing these activities, which has been described by so many investigators was completely lacking; no periodicity in the bodily functions could be observed, so that menstruation, in these cases at least, must be considered as a completely normal process, exerting no appreciable influence on the organism as a whole.

Treatment of Sterility.—NORRIS (*Surg., Gyn., and Obst.*, 1912, xv, 706) reports exceedingly satisfactory results in the treatment of certain cases of sterility in women by the use of his modification of the Wylie drain. This, a form of stem pessary, having a well-marked groove on each surface, and a T-shaped lower end, the arms of the T resting against the outer surface of the cervix when the drain is in place, and being held there by silk ligatures placed through a small hole, provided for that purpose at the end of each arm, and taking in a bit of the cervical tissue. The stem, which has a bulbar enlargement on the inner end, should be of such length as to reach to within 1.5 cm. of the top of the uterine cavity. The technique employed by Norris in the use of this pessary is merely to give the cervix a thorough dilatation, taking at least fifteen minutes for this, and then to introduce the drain, after exploring the interior of the uterus for the possible presence of a polyp or small myoma. The instrument may stay in place for six weeks, during which time no douches should be taken by the patient. The presence of the drain is no contraindication to the resumption of sexual relations, however; indeed, in three of Norris' cases, conception apparently occurred while it was in place. Norris emphasizes that this form of treatment should be used only in those cases where sterility is present with no other pathological condition than a small cervical canal. Where the slightest suspicion of any inflammatory condition exists, it is absolutely contraindicated. By its use, Norris reports a cure in 13 out of 35 cases whose histories subsequent to the operation could be traced, giving a ratio of 37 per cent., but since a number of the patients in whom pregnancy has not as yet ensued have been operated on within the last year, it is reasonable to suppose that this percentage may be somewhat increased.

Occurrence of Sarcomatous Degeneration on Uterine Myomas.—An unusually high percentage of myomas showing beginning sarcomatous change is reported by WARNEKROS (*Arch. f. Gyn.*, 1912, xcvi, 292) from Bumm's clinic in Berlin. He has subjected their last 78 cases of myoma to very thorough microscopic examination, as a result of which he has found areas which he considers carcinomatous in no less than 7, corresponding to almost 10 per cent. He admits that this is much higher than the average reported by most observers, which at the present time appears to be about 4 or 5 per cent., and also that this series of cases is too small upon which to assume that such a high percentage of malignancy represents the true state of affairs, but he also insists upon the fact that this percentage is steadily increasing as it is becoming the routine practice of many clinics to subject all myomatous tumors to a much more thorough routine examination than formerly. These areas may be extremely small, and since they do not occur in any definite portion of the myoma, it is not

unreasonable to assume that they be frequently overlooked when only one or two small pieces are taken from a large tumor for microscopic examination. An extremely practical side to the determination of the true proportion of myomas which undergo malignant change is furnished, he thinks, by the increasing tendency, at least on the part of many of the German clinics, to subject these patients to x-ray treatment rather than to operation; if it can be shown that malignancy occurs in the long run in these tumors with anything like the frequency that he has apparently demonstrated, general adoption of x-ray therapy in place of extirpation must of necessity be associated with a very great element of danger for a considerable proportion of the patients.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Chloroma.—A. M. BURGESS (*Jour. Med. Research*, November, 1912, xxvii, No. 2) reports 2 cases of chloroma, and reviews the subject. It will be remembered that the striking characteristic of this so-called disease, which is relatively a rare one, is the greenish color of the tumor. Burgess has found some 80 cases reported. Nothing new is at hand regarding the coloring matter, which is by some supposed to be a lipochrome. The author finds that the tumors called by this name do not constitute a pathological entity, but are a manifestation of one of the types of acute myelogenous leukemia; no connection with lymphatic leukemia has yet been demonstrated. Myelogenous leukemia is thus to be considered as the metastasis in the blood of a neoplastic growth in the bone marrow, and in cases where the cells are little differentiated, their power of growth is so great as to permit definite localized masses to occur; these growths, if possessed of the characteristic green color, are designated by the term chloroma.

Smallpox.—FISCHER-DEFOY (*Schmidt's Jahrb.*, October, 1912, Band ccxvi, Heft 1) has collected current literature upon smallpox, vaccination, and kindred subjects, with the usual results; as always, it is mortifying to see the position occupied by English-speaking nations in the morbidity statistics, and to be compelled to accept the patronizing, if good-natured smile, that circumstances allow the continental nations to bestow. In Germany, during the fourteen years previous to 1910, there were 3348 cases of smallpox, of whom 27 per cent. were foreign. England's yearly death-rate, according to House of Commons statistics is 600 to 800, and the United States (possibly including Canada), in 1910 showed 30,000 cases. In Prussia in 1908, the death-rate comprised 7 per cent. of the vaccinated and 47 per cent. of the unvaccin-

ated. For one year, Bavaria shows 8 cases of smallpox, Saxony, 19. Great Britain does better for her colonies than for herself, for while in India during the seventeen years preceeding 1886, 45,000 died of smallpox, in the seventeen succeeding years, 9126 died. On the European continent, Russia still shows the greatest proportion of cases, if Great Britain be excepted, and the result of vaccination in the Philippines has shown most satisfactory results.

Comparative Toxicity of Methyl and Ethyl Alcohol.—The occurrence of large numbers of fatal cases of methyl alcohol poisoning gives interest to the experiments of NICLOUX AND PLACET (*Jour. de Phys. et de Path. gén.*, September, 1912, vol. xiv, No. 5), with regard to its toxicity in comparison with ethyl alcohol. In a single large dose given intravenously methyl alcohol is the less toxic, but at death there is a greater proportion found in the blood and the tissues; of the tissues the brain is the most arid in fixing either form of alcohol. If the alcohol be ingested and repeated doses, methyl alcohol is the more toxic, because it is capable of less complete combustion, and is eliminated more slowly; a quarter of the methyl alcohol ingested is found to be in the excretions and the excretory organs. In spite of these facts, Nieloux and Placet considers that it is necessary to invoke the impurities of methyl alcohol to explain the numerous fatal cases unless it can be proved that man has a particular susceptibility to the action of the drug.

Bone Lesions in Skeletons of Ancient Peoples.—RUFFER AND RIETTI (*Journal of Pathology and Bacteriology*, April, 1912), publish the results of their examinations of ancient skeletons. The former had previously studied the histology of Egyptian mummies, and is deeply interested in the unusual field that is thus opened for investigation. Most of Ruffer and Rietti's good specimens will be placed in the Medical School Museum at Cairo, but a considerable number of bones will remain for distribution to recognized pathological institutes which may apply for the same. The earliest skeletons date from 3000 B.C., and show spondylitis deformans as well as other osteo-arthritic lesions in the hands, sacro-iliae articulations, hip-joints, and other parts. It is remarkable how numerous were the lesions of this type found in these skeletons; nor were the results very different when skeletons from the Roman period, 200 A.D., were examined, for here of 8 skeletons, no less than 4 showed marked lesions of arthritis deformans. Ruffer and Rietti find themselves unable to offer even a guess as to the etiology of these osteo-arthritic lesions. Should we ever discover more about the bacterial diseases of Ancient Egypt we shall perhaps be able to indicate the cause of this widespread disease. Ruffer and Rietti found a certain number of cases in the young, but point out that it was essentially a disease of old age, because, in hieroglyphic writing, the symbol of old age was a man deformed by chronic arthritis. Attention was paid to an attempt to determine the extent to which disease of the teeth prevailed in ancient times, and Ruffer and Rietti, after examination of a large number of skeletons, are of the opinion that there seems to have been much the same distribution of dental disease then as there is now. Although the Egyptians were learned in dentistry, there is evidence that they frequently failed to pull out teeth which prevented the exit of abscesses, for

Ruffer and Rietti have seen the results of abscesses which had ruptured through bone but for which no teeth had been removed, although such removal was most obviously indicated. No evidence is forthcoming from the present writers that the Egyptians knew anything about filling teeth, and they further state that they have only once seen ancient artificial teeth, which were found in a Roman tomb in Egypt. The contrivance consists of teeth bound together by gold wire, and was evidently for show purposes as it could not possibly have been used for mastication. The use of the tooth brush or some such instrument was evidently widespread, and the teeth in most cases showed evidence of careful attention, deposits of tartar being extremely infrequent.

The Pineal Body.—A review of the literature dealing recently with the pineal body is given in part in the *Medical Chronicle* for December, 1912, by L. J. KIDD. Some of the conclusions already made are as follows; there is a general belief that the pineal body is functional in all vertebrates and little evidence to show that it is a rudimentary, degenerated, or disappearing organ. Although there is no evidence that is sufficiently clear, it seems to be a fair assumption that it furnishes an internal secretion which probably in young birds and mammals at least, has an inhibitory action on the development of the testes and body growth, and on the appearance of secondary sexual characters. The relationship of the pineal glands to the ovaries is suggested but not yet proved: the relationship with the pituitary and the cortex of the adrenal is probable, but is yet uncertain. Involution of the pineal body occurs normally at puberty, but it is likely that the organ has other functions than these prepuberal effects. The histology of the organ with its neuroglial and connective tissue elements suggests definite specific function apart from that already stated.

Studies upon Pneumococcus.—From the Hospital of the Rockefeller Institute (*Jour. Exp. Med.*, November 1, 1912), comes an interesting series of studies upon pneumococcus to which brief reference may be made. COLE has studied the toxic substances produced by the pneumococcus, with the result that he finds that filtered blood serum of strongly infected animals is itself not necessarily toxic. Extracts from the organisms kept in salt solution for varying periods of time do not prove to be uniformly toxic, nor has Cole been able to discover the exact circumstances under which they prove so. Deaths from injection of such solutions suggested the results seen in acute anaphylaxis. The peritoneal washings of infected guinea-pigs injected into the circulation proved fatal in a considerable percentage of all cases, the symptoms again being those of acute anaphylaxis, which form of death becomes all but an absolute certainty when pneumococci are dissolved in solutions of bile salts and injected intravenously, a result which is probably due to the setting free of substances from the bacterial bodies in the rapid solution which the pneumococci undergo in bile at body temperature. DOCHEZ has examined the protective substances to be found in the serum of patients recovering from pneumonia. He finds that the appearance of protective bodies in the blood may coincide fairly well with the time of crisis and the disappearance of symptoms. While they are not measurably in the blood before

crisis, they may be proved in considerable quantity subsequent to that phenomenon, and yet in some cases it is impossible to demonstrate them at any period of the disease. When the serum has been tested against its homologous strain of pneumococcus most cases show that it contains protective bodies, but if the test be made against stock cultures no such quality is observed. Doehez has further studied the occurrence of pneumococcus in the circulating blood and found it in approximately half of the 37 cases studied. The course of infection when the pneumococcus was found in the blood was more severe than in those in which it could not be cultivated. Seventy-seven per cent. of patients with positive blood cultures died, and 79 per cent. of patients with negative blood cultures recovered. In fatal cases where the pneumococcus was found in the blood, its numbers rose shortly before death to enormous figures; on the other hand when blood infection was not demonstrable, fatal cases were characterized by a very rapid spread of consolidation in the lungs, and Doehez considers that the symptoms of collapse which may develop on the fifth or sixth day of lobar pneumonia, often mark the invasion of the blood by the organism; or if not this, then a marked extension of the consolidation of the lung. The pneumococci were usually virulent to animals, although in some cases with recovery they seemed to possess but a relatively low virulence. Doehez tested a univalent serum against 19 strains of typical pneumococcus, and against 4 strains of allied organisms. The serum showed some protection against 12 out of the 19, but none against the allied organisms, and the majority of the successful cases showed a high degree of protection. Doehez has further published his experiments in the coagulation time of the blood in lobar pneumonia, and finds that the time is prolonged during the acute stage, returning to normal during convalescence. The lengthening of coagulation time he considers due to an increased formation of antithrombin in the liver, which organ he also considers responsible for the similar increase in quantity of circulating fibrinogen. PEABODY has studied the carbon dioxide content of the blood in pneumonia, and finds its diminution to be all but a constant feature; it tends to be lowest in bad cases and in terminal stages, but no constant relationship exists between its amount and the severity of the disease, nor does the diminution of carbon dioxide bear any apparent relation to temperature; the diminution may even persist for a considerable time after the fever has disappeared, and appears to be one more evidence of the metabolic changes existing in infections which are by no means confined to the febrile period of the disease. The carbon dioxide content of the blood ran parallel to the output of ammonia in the urine, but does not appear to have any relation to excretion of chlorine.

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ORIGINAL ARTICLES

CONCERNING THE SYMPTOMATIC DIFFERENTIATION
BETWEEN DISORDERS OF THE TWO LOBES
OF THE PITUITARY BODY:

WITH NOTES ON A SYNDROME ACCREDITED TO HYPERPLASIA OF
THE ANTERIOR AND SECRETORY STASIS OR INSUFFICIENCY
OF THE POSTERIOR LOBE.¹

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INTRODUCTION. It is to the credit of clinicians that our knowledge of the disorders of the various ductless glands has originated, in most instances, from studies made at the bedside. Only under the spur of these primary clinical observations have the physiologist, the morbid anatomist, and the experimental pathologist—not rarely in the person of the physician himself—been led to make their important though supplementary investigations.

Rapid as our advance has been under these combined efforts, it is to be noted that with but one or two exceptions our acquaintance with these disorders of an internal secretion is limited to those states brought about by a primary diminution, rather than increase, of functional activity of one or another of the cellular structures in question.

Thus Addison attributed the syndrome which bears his name to a destructive lesion of the suprarenal capsules; the observations of Gull and Kocher served to make clear the clinical manifestations of thyroid incompetency; tetany has become recognized as

¹ Read in the Symposium on Internal Secretions at the meeting of the American Medical Association, held at Atlantic City, June, 1912.

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an expression of parathyroid insufficiency; certain forms of diabetes are associated with lesions compromising the pancreatic islets; and mutilating operations on the generative organs have long since familiarized us with the constitutional manifestations due to the deprivation of ovarian and testicular products of internal secretion, even though there remains much confusion in regard to the individual significance of the various cellular elements, interstitial and epithelial, the loss of which elicits the resultant syndrome.

In short, the recognized clinical expressions of disordered function of one or another of these structures lie on the side of secretory insufficiency, with the exception of the Graves-Basedow syndrome, in the case of the thyroid gland, and Marie's acromegaly, in the case of the pituitary body. Indeed, the latter disorder was originally ascribed to a lowered secretion, and for years futile attempts were made to reproduce the condition by glandular extirpations in animals.

Each member of the ductless gland series is doubtless susceptible, within normal physiologic limits, to a wide range both of increased and diminished functional activity; and during certain periods of physiologic stress, as in adolescence, pregnancy, and the climacteric, as well as in many conditions of disease, clinical evidences of these changes in activity may be apparent. Particularly in an individual in whom there is a tendency, inherited or otherwise, to a chemical instability of one or another of the glands, these functional fluctuations, with which we are becoming more and more familiar, in the case particularly of the thyroid gland, may overlap the pathologic so far as to give constitutional symptoms which may deserve the name of a definite malady.

With full appreciation of the close physiologic correlation of these structures—either through chemical or autonomic nervous interactions—and consequently of the polyglandular character of the syndrome aroused by a profound disorder of any individual member of the series, nevertheless there can be no doubt but that *there exists a characteristic and recognizable syndrome for a primary derangement of each individual gland, whether on the side of its secretory overactivity or of its secretory underactivity.* Furthermore, in the progress of many of these disorders, transition conditions are to be expected, and if the constitutional derangement of an earlier state, let us say of overactivity, has led to fixed somatic changes, we may anticipate clinical combinations of the opposed states, the one due to a perversion or excess of secretion and the other to a diminution or loss of secretion.

Disorders of the thyroid gland have heretofore furnished the only fairly clear example of these counterposed and transitional states, but the derangements of hypophysial function are rapidly coming to the front, for in the case of this gland also we have learned

to distinguish between the clinical evidences of an excess or perversion of secretion and those of insufficient secretion. Moreover, there are suggestions that we shall soon come to recognize clinically the constitutional effects of pathologic hyperplasia of other of these structures—adrenals, thymus, and pineal gland, as well as interstitial cells of testis and ovary—whose known disorders are now restricted to the conditions resultant upon states of insufficiency alone.

HYPOPHYSIAL DISORDERS. In a recent presentation of some observations on a series of patients suffering from variable derangements of the pituitary body,² it was fully appreciated that the constitutional manifestations which were there attributed either to a secretory excess or deficit were roughly ascribed, in the majority of cases, to a disordered function of the gland as a whole. Since the gland is in reality a dualistic organ, its two lobes possessing properties of great functional divergence, it is natural that we should begin to look for clinical expressions of derangement of one or the other portion. It is this topic which I shall consider on this occasion.

Though many hypotheses have been advanced in regard to the primary pathologic lesion which incites the clinical expressions of acromegaly and gigantism—maladies whose striking phenomenon is skeletal overgrowth—it has become generally conceded not only that the overgrowth is consequent upon a hypophysial derangement, but that a functional hyperplasia of the gland is the underlying factor.

The many arguments which have accumulated in favor of this view, as opposed to the original assumption of Marie, need not be assembled here, but possibly the one which is most conclusive—though admittedly a negative argument—is that experimental ablation of a large part of the pituitary body in preadolescent animals leads to a striking failure of skeletal development. For some experiments conducted with my associates, Crowe, Homans, and Goetsch in the Hunterian Laboratory, first gave us an insight into the nature of the syndrome to which general attention was primarily drawn by Fröhlich—a syndrome in which a tumor of the hypophysis or its vicinity, in the comparatively young, is accompanied by lack of full skeletal development, by adiposity, and by the failure of full secondary sexual characteristics to appear.

Our experiments showed that these clinical states, which were immediately recognized by all as familiar ones, whether or not they were accompanied by actual tumor manifestations, were due to a hypophysial insufficiency; for many of the laboratory animals, when deprived of a large part of the gland, became obese, remained undersized, and failed to acquire their normal sexual

² *The Pituitary Body and its Disorders*, Philadelphia, 1912.

adolescence if puppies, or lost some of the attributes of adolescence if these had previously been acquired. It becomes obvious therefore that the local tumor in the clinical cases is but an incident, the effect of which has been to interfere with the gland's activity, and that the same syndrome may be expected as the result of a primary hypoplasia in the absence of tumor. This is equally true of thyroid disorders, for a tumor or enlargement of this gland, though not an uncommon accompaniment of cretinism or myxedema, is by no means essential to the process or to its recognition.

Our earlier experimental studies were directed toward the determination of the essentiality of the hypophysis to life,³ a matter which after all is of no great moment, provided the importance of the structure to the maintenance of physiologic equilibrium is conceded; and at the time of our earlier experiments it was a general impression that the gland was of no vital importance. The experiments therefore concerned themselves largely with the effect of total or partial ablation of the gland as a whole; and in explaining the results we were led to lay too great stress on the function of the anterior lobe.

Subsequent studies conducted on another series of animals, with Goetsch and Jacobson, led to the conclusion that, apart from the growth factors, the symptoms of deficiency which we had observed were with greater probability due to an interference with the secretion of the posterior lobe—the portion of the gland which had long been shown by physiologists to contain active substances. It was found that the constitutional evidences of glandular insufficiency could be produced by the mere obstruction of the hypophysial stalk; and thus we have come to hold the view, which we believe, in spite of some controversion, to be supported by experimental as well as clinical evidence, that the secretion of the posterior lobe finds its way into the cerebrospinal fluid.

On this conception, therefore, stripping the subject of all details, the strictly epithelial portion of the gland, or *pars anterior*, is a typical ductless gland, which discharges its secretion into the large sinusoidal blood channels which traverse it. It is chiefly related to factors of skeletal development, and may be considered to elaborate a hormone capable of stimulating growth. On the other hand, the neuro-epithelial *pars posterior* is, in a sense, a gland of external secretion, its active principle or principles reaching the blood stream by way of the cerebrospinal fluid.

The posterior lobe, moreover, is closely related to metabolic processes, and particularly to the assimilation of the carbohydrates. A deficiency of its secretion, whether produced by experimental

³ Concerning this point the interpretations of Paulesco and of Crowe, Cushing, and Homans (Bull. Johns Hopkins Hosp., 1910, xxi, 127) have been controverted by Handelsmann and Horsley (British Med. Jour., 1911, ii, 1150) and by Aschner (Arch. f. d. ges. Physiol., 1912, cxlvi), using a different operative approach.

ablation of the gland or by obstruction of the infundibular stalk, or by a pathologic lesion—tumor or otherwise—which produces a corresponding secretory loss or stasis, leads to a noticeable increase in the tolerance for sugars, with associated tendency to adiposity, a subnormal temperature, somnolence, dry skin, polydipsia, and polyuria, loss of hair, characteristic psychic, often epileptiform, disturbances, and so on—a sort of “pituitary myxedema,” as it were. An excess of posterior lobe secretion, on the other hand, whether the result of some functional disorder or due to the over-administration of extracts, causes tissue waste with loss of flesh, a relative intolerance for carbohydrates, often with spontaneous glycosuria, a moist skin, etc.—symptoms, in other words, the reverse of those recounted above.

Moreover, in each case symptoms referable to a secondary derangement of other ductless glands occur, more notably on the part of the generative organs, with an apparent activation when there is hypophyseal hyperplasia, and unquestioned anaphrodisia—even lack of development or atrophy—when there is hypophyseal hypoplasia; and it is possible that this pituitary and gonadal relationship is more intimately a posterior than an anterior lobe effect, though this is a matter of present conjecture.

Now in our series of carefully observed examples of hypophyseal derangement, which at the present writing comprises over 60 cases, it has seemed that some clinical differentiation between a disordered function of the two lobes was possible, not only in some of the patients with typical and outspoken manifestations of acromegaly—a condition ascribed to glandular hyperplasia—but in others as well who presented manifest adiposogenital dystrophy—a condition ascribed to glandular hypoplasia. Moreover, there have been a number of clinical types which have conformed neither with the typical syndrome of Marie nor with that of Fröhlich—types, as we shall see, which suggest a functional hyperplasia of one lobe with lowered activity of the other.

1. *The Acromegalic Syndrome.* On the assumption that overgrowth is related to a pathologic hyperplasia of the anterior lobe which expresses itself as more or less pronounced gigantism if the disorder occurs before ossification of the epiphyses, or as more or less pronounced acromegalic changes if epiphysal union has already taken place, it has been of interest to find that all but 3 of the 14 pronounced acromegalics of our series, at the time they came under observation, were exhibiting evidences of what we regard as a posterior lobe insufficiency. They were acquiring some measure of adiposity; they all possessed a high, often an exceedingly high, tolerance for sugars; they showed a tendency toward somnolence, a subnormal temperature, anaphrodisia, and the rest. On the other hand, in the earlier stages of acromegaly, or in periods of exacerbation of the disease, there is apt to be a reverse picture,

with an active metabolism, of which spontaneous glycosuria is a not infrequent expression.

These observations therefore suggest that a hyperplasia of both lobes of the gland occurs during the acute stages of the malady, whereas with the further advance of the disease there is a tendency at least for the posterior lobe, and possibly for the *pars anterior* as well, to undergo such retrogressive changes as to leave the structure functionally deficient.

Radiographic studies of the cranial base of all acromegalics show an enlargement of the pituitary fossa, even though the hypertrophic gland, in the majority of instances, fails to reach such a size as to produce neighborhood pressure symptoms. During the progress of the disease, however, the gland is capable of such involutional changes that it may no longer fill the enlarged fossa, and may, indeed, on chance postmortem examination, be found to present no apparent gross or microscopic abnormalities whatsoever. On this basis are easily explained the occasional reports which have been made of acromegalics who have succumbed to intercurrent diseases and in whom the hypophysis has shown no apparent deviation from what is regarded as normal—certainly no hypertrophic enlargement.

2. *The Syndrome of Dystrophia Adiposogenitalis.* In typical examples of this syndrome of Fröhlich it is natural to assume that a pathologic hypoplasia of both parts of the gland has occurred. In most of the cases heretofore recorded the lesion has been shown to be either an interpeduncular cyst containing squamous epithelial elements, or a teratomatous growth arising from an anlage related to the original pharyngeal pouch which serves to compress the gland directly.

In the typical cases, moreover, the symptoms date from a pre-adolescent era, and as a consequence of the anterior lobe implication the stature remains small. On the other hand, the adiposity and its allied evidences of lowered metabolic activity, which have been recounted above, indicate a coincident posterior lobe obstruction, to which, likewise, the genital dystrophy with imperfect acquirement of secondary characteristics of sex may also point.⁴

We see therefore that these two syndromes in their typical form correspond, in the case of acromegaly, with an apparent secretory activation of both lobes of the gland, at least during the early

⁴ It is to be emphasized, of course, that the so-called syndrome of *adiposogenital dystrophy* may first appear in adult life when full stature has been acquired. Moreover, it need not be associated with tumor. Traumatic hypophysial lesions, for example, may lead to the same syndrome through actual glandular destruction—a condition comparable to the experimental reproduction of the syndrome in adult animals by extirpation methods. It is to be noted, furthermore, in the cases in which tumors are actually present, that adiposity with high sugar tolerance is not inevitable, for *there are lean as well as fat types of these individuals*. However, in the examples of the former which have come under our care the reproductive powers have not been impaired, despite the imperfect secondary characteristics of sex shown by absence of pubic and axillary hair, etc. The adipose types, on the other hand, have usually been impotent.

stages or subsequent exacerbations of the disease; whereas in the syndrome of Fröhlich there is a primary and chronic lowering of activity of both anterior and posterior lobes, the result of direct compression.

Now, in the production of one or the other of these syndromes it is not impossible that one lobe alone of the gland may be functionally deranged. Thus it is conceivable that the essential features of acromegalic overgrowth may be occasioned by an hyperplasia in which the anterior lobe alone participates. On the other hand, it is beyond conjecture that lesions limited in their effect to the posterior lobe may give clinical symptoms. This, as we shall see, is a particularly common sequel of hydrocephalus, but it may occur, as well, as a consequence of the very type of growth acknowledged to be a common cause of the typical syndrome of Fröhlich.⁵

In our series of cases of brain tumor, symptoms suggestive of hypophysial insufficiency have occurred with such frequency that it has become a routine of history-taking to assemble them apart from the strictly neurologic findings. Moreover, in the routine examination of fatal cases in which the central nervous system has been hardened *in situ*, it has been observed that more or less flattening—"saucer deformation"—of the pituitary body is a common finding, particularly with an internal hydrocephalus involving the third ventricle.

On the presumption that the posterior lobe of the gland discharges into the cerebrospinal fluid, hydrocephalus may be expected to cause a mechanical retention of the products of secretion of this part of the gland; and we have thus come to explain the adiposis, subnormal temperature, and high sugar tolerance which these patients often exhibit. In other words, a distant lesion with secondary ventricular hydrops is equivalent, in its effect on the posterior lobe, to the actual experimental obstruction of the hypophysial stalk or to the direct pressure of a superimposed (infundibular) tumor.

3. *The Syndrome of Overgrowth with Adiposity.* The anterior lobe, under the circumstances recounted above, may remain unaffected, as the vascular channels into which it discharges need not be seriously compromised. Under certain conditions, however, it may seemingly respond, by a hyperplastic reaction, to these pressure effects transmitted through the cerebrospinal fluid, and thus a definite acceleration of growth may accompany the

⁵ We have had one straightforward example of this with postmortem confirmation. A young adult with moderate adiposogenital dystrophy and bitemporal hemianopsia showed no skeletal changes whatsoever, and the x-ray disclosed a normal sella turcica. The patient died from an intercurrent malady, and at autopsy a typical squamous-celled cyst of pharyngeal duct origin was found situated on the infundibular stalk well above the sella, which was of normal configuration and contained an average-sized, undeformed gland. The anterior lobe was normal, whereas the posterior lobe showed the characteristic cellular appearance of obstruction.

adiposis, increased sugar tolerance, and other symptoms attributed to the posterior lobe stasis.⁶

A notable example of this was seen in an adult patient with a large cerebellar cyst (unsuspected and found at autopsy) in whom an acute acromegaly supervened during the progress of the cerebellar lesion, which eventually led to a ventricular hydrocephalus.⁷ Doubtless the adult skeleton is relatively insusceptible to the stimulus of the hormone of growth; and so far as I am aware this is the only recorded example of the combination of hydrocephalus secondary to tumor with resultant enlargement of the acral parts of the body. In the case of the young, however, it is otherwise, and in our brain tumor series many examples of rapid growth combined with adiposity—in other words, of presumed hyperplasia of the anterior lobe with lowered posterior lobe activity—have been observed.

It is particularly important, however, that we should learn to recognize these clinical expressions of hypophysial disorder in the absence of brain tumor symptoms or radioscopic enlargement of the pituitary fossa, in the same way that it is important for us to recognize thyroid disorders unaccompanied by gross evidences of change in the configuration of the gland.

Hence the following three recent examples have been chosen to illustrate the symptom complex under discussion. The first would pass for the *typus Fröhlich* were it not for the overgrowth and the absence of tumor. The physical type is not an unfamiliar one.

CASE I.—*Adiposogenital dystrophy, with epilepsy and overgrowth.*

March 4, 1912. Charles H., aged ten years, admitted with the complaint of epilepsy and adiposity.

He is the eldest child; born after a prolonged labor; birth weight, fourteen pounds.

He has had epilepsy since his first year. The attacks are severe and frequent, often ten or more a day. Nevertheless, he is of average intelligence, and attends school with children of his own age, and stands well in his classes.

Following an attack of typhoid three years ago there was a marked change in his dispositional and other characteristics. From being tractable he has become an irritable and stubborn child. He has grown rapidly in height and has become very obese, though he was always large for his age.

⁶ It should not be overlooked in this discussion that similar mild grades of skeletal overgrowth or incipient gigantism occurring in conjunction with adiposity have been attributed by Marburg and Frankl-Hochwart to lesions (tumors) of the pineal gland; but these cases are characterized by a remarkable precocity of adolescence, with early acquirement of secondary characteristics of sex, whereas tardy and incomplete manifestations of sexual adolescence characterize the hypophysial group. Moreover, as I have pointed out in the discussion of a case of supposed pinealism of this type, internal hydrocephalus with secondary hypophysial implication is inevitable with a pineal tumor of any size, so that a composite pineal and hypophysial glandular syndrome may be anticipated. A certain measure of *Frühreife* may occur with hypophysial lesions which are presumably primary, as in Case III of the present report.

⁷ Loc. cit., "The Pituitary Body and its Disorders," Case XXXVIII, p. 194.

Physical Examination. A light-complexioned, oversized, petulant, fat boy (Figs. 1 and 2), weighing 70 kilo., or 155 pounds (normal for his age, 30 kilo., or 66 pounds), and measuring 149 cm. in height (normal average, 132 cm.). He therefore stands 17 cm. ($5\frac{3}{4}$ inches) and weighs 40 kilo. (89 pounds), more than the average boy of his age.⁸



FIGS. 1 and 2.—Case I. Overgrowth, with adiposity. Patient on left contrasted with boy of same age and average height. Weight, 155 pounds (average normal, 66 pounds).

Neuromuscular, visceral, renal, arteriovascular, and other systems negative. Blood and urine negative.

There are no definite pituitary *neighborhood symptoms*, though in some respects his attacks suggest uncinat fits. There is a slight left abducens palsy. A cranial radiogram shows a small sella

⁸ Boas' tables, *Science*, April 12, 1895.

perched on a solid (non-cellular) sphenoidal base. The head is not large (54 cm.); there is no internal hydrocephalus.

The skeletal configuration and the disposition of the panniculus are of feminine type (Figs. 1 and 2). Circumferential measurements are as follows: over pectorals, 97 cm.; at umbilicus, 104 cm.; over hips, 99 cm.; thigh, 61 cm.; calf, 38 cm.

Aside from the overgrowth and adiposity the *hypophysial symptoms* are not very conspicuous. The skin is delicate, smooth, and hairless except for the normal growth on the scalp. The temperature is subnormal, ranging from 96° to 98°. The assimilation limit for levulose is high, 200 grams giving a bare trace of sugar in the urine. No polyuria.

There is no clinical evidence of derangement on the part of the other glands of internal secretion, except that the genitalia are abnormally small.⁹

In physical appearance this boy is the exact counterpart of another patient whose case has been reported in greater detail¹⁰ as one of *dystrophia adiposogenitalis*. In both instances there occurs the same type of sella perched upon a solidified instead of the usual cellular sphenoidal base, and we have observed a similar condition in a number of other epileptics. In both cases, furthermore, the administration of glandular extracts apparently served to check the epileptiform seizures, which seemingly bear some relation to pituitary insufficiency, as has been elsewhere emphasized. Glandular therapy, however, has not so effectually overcome the tendency to adiposity in this, as it appears to have done in the patient more fully reported in my monograph.

The following two patients are physical counterparts of one another in so far as their ductless gland symptoms are concerned. One of them, however, is suffering from a primary brain tumor to which the hypophysial disorder is secondary; in the other there are no unequivocal tumor manifestations.

CASE II.—General pressure phenomena, with secondary hypophysial symptoms, overgrowth, adiposity, sexual dystrophy.

May 24, 1912. Leon S., aged sixteen years, a schoolboy, referred with the complaint of headaches and a possible diagnosis of pituitary disorder.

He is an only child. Until his present illness he has always been vigorous and athletic. About six years ago he received a cranial injury, followed by unconsciousness; this has left a scar on his forehead.

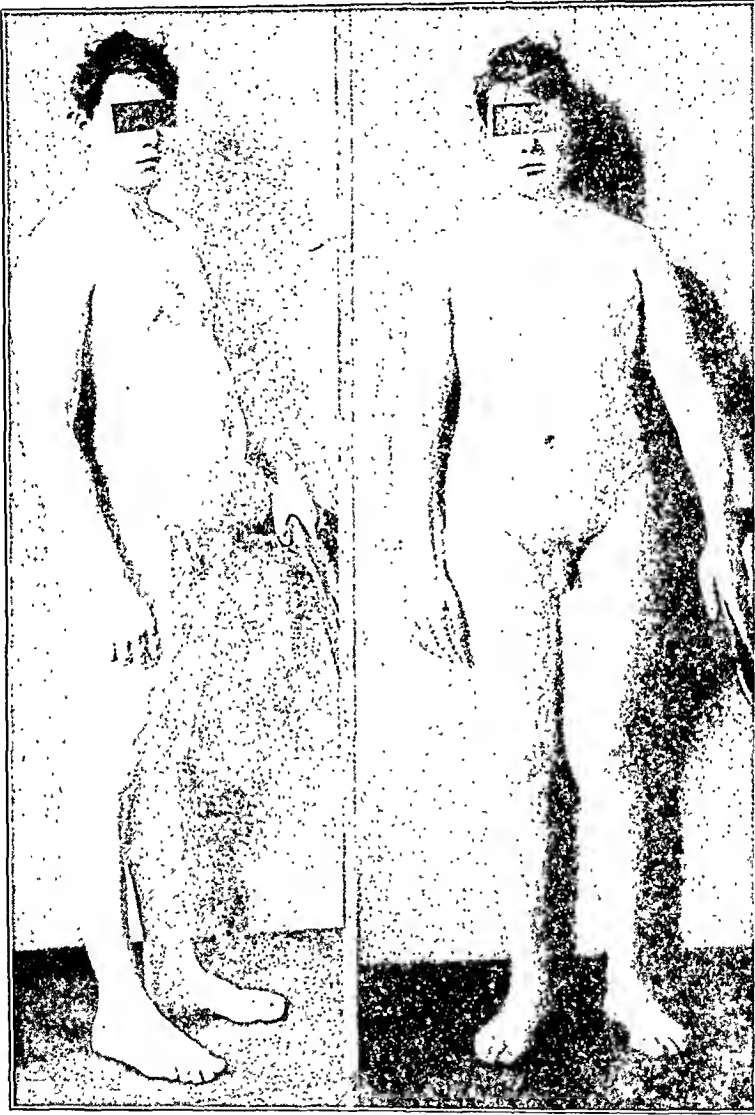
Present Illness. He began having frontotemporal headaches nine months ago. Coincidentally he acquired a ravenous appetite, especially for sweets, and during the following six months his

⁹ Pituitary feeding was instituted, and there have been no seizures up to the time of this writing (an interval of three months).

¹⁰ Loc. cit., "The Pituitary Body and its Disorders," Case XXXIV, p. 175.

weight increased from 133 to 205 pounds. A rapid growth (estimated at three inches) occurred during the same period. Polyuria and polydipsia were also pronounced.

Six months ago he had a severe illness of three weeks' duration, with fever, cough, rusty expectoration, great accentuation of his



FIGS 3 and 4.—Case II. Overgrowth, with adiposity in association with brain tumor. An increase of 2 inches in height and 72 pounds in weight in nine months.

headache, drowsiness, and stupor. There have been several recurrences of a similar nature, always with bursting headache, some delirium, and fever.

These recurring attacks, with polyuria, polydipsia, and polyphagia, and a constant increase in weight, continued until three months ago. Since that time a vigorous treatment with thyroid extract has been instituted, and under it he has lost 20 pounds.

He has become more and more drowsy, stuporous, and indifferent. His memory has become impaired, his statements are unreliable, and orientation for time and place seem uncertain. There have been periods of diplopia. He has had hallucinations of sight and sound; and hiccoughing, nausea, and vomiting have accompanied the more severe recent headaches.

Physical Examination. An overgrown, abnormally boy, with a peculiar grayish, edematous-looking, and almost hairless skin. Temperature and pulse slightly elevated. Blood pressure 110. Visceral (cardiovascular, thoracic, and abdominal) examination negative. Blood (Wassermann), cerebrospinal fluid, and urine negative.

Symptoms of intracranial tension are pronounced. Aside from the headaches and vomiting there is a choked disk of 3 D. on the right and 2 D. on the left. The *neurologic examination* shows, further, a weakness of the left abducens, increase in the deep reflexes throughout, with ankle clonus and a positive Romberg sign. Psychic disturbances are profound, with loss of memory, extreme drowsiness, apathy, and some disorientation. The cranial röntgenogram shows large diploëtic channels and slight separation of the sutures characteristic of internal hydrocephalus.

Analysis of Hypophyseal Symptoms. (a) *Neighborhood:* The sella is of normal outline, possibly slightly enlarged (1.4 cm. by 0.8 cm.). There are no local pressure disturbances.

(b) *Secretory.* The body configuration is of a feminine type, with broad hips, genu valgum, and tapering extremities. Height is 170.6 cm. (5 feet 7½ inches). Circumferential measurements: thorax, 96 cm.; abdomen, 98 cm.; hips, 106 cm. (Figs. 3 and 4).

Cutaneous. The skin shows a peculiar, cadaverous pallor, though the blood gives 86 per cent. of hemoglobin. Its appearance is not unlike that in cases of nephritis with edema. It has a slightly more yellowish tinge, however, than in some of the pronounced cases of hypopituitarism that we have seen. It is soft, fine, and delicate. There is a slight axillary moisture, but the extremities are exceedingly dry.

Hirsuties. With the exception of the scalp and a slight growth of hair with feminine distribution on the pubes, the body is hairless. The patient has never shaved.

Subcutaneous. The fat is abundant, particularly over the hips, thighs, and pectorals. It is tender, even on slight pressure ("adiposis dolorosa"). There is some pigmentation around the neck in the axillæ, and between the symphysis and umbilicus is a pigmented line similar to that seen in pregnant women. There are many lineæ atrophicæ over the hips.

Polyuria and polydipsia were formerly marked symptoms. Pulse and respiration are not subnormal—indeed, there is a slight elevation. Blood pressure, 110. Apathy, drowsiness, and stuporous

periods are characteristic features. *Sugar tolerance* is not determinable, as amounts of levulose over 150 grams cannot be retained.

Other Ductless Glands. Adrenals: Asthenia and pigmentation. Thymus: Some increase in retrosternal dulness, extending about 4 cm. to the left of the sternum and over the first interspace at the right; no lymphatic enlargement. Testes: Decidedly smaller and softer than normal.

Diagnosis. Brain tumor, possibly cerebellar, with low grade of internal hydrocephalus and secondary functional pituitary disturbances.

Operation. June 1, 1912. Right subtemporal decompression. Subsequent lowering of choked disk to 1 D., with considerable improvement in other respects. Patient discharged June 20.

The clinical picture in the following case is very similar, so far as the growth and adiposity are concerned, though in this instance there are no certain tumor manifestations.

CASE III.—*Overgrowth, adiposity, hypertrichosis.*

June 7, 1912. Donald S., aged sixteen years, admitted with the complaint of overgrowth, lowered mentality, and adiposity.

Family history without record of abnormalities, unusual stature or corpulence.

Personal History. A normal, ten-pound, breast-fed baby. Has had measles, chickenpox, and mumps. Always somewhat over-large for his age. Otherwise normal in all respects until his ninth year. Regarded as a bright and intelligent boy, in advance of his age, at school.

During his eighth year he acquired an abnormal appetite and became exceedingly adipose. His abdominal panniculus at this time is said to have been enormous.

At eleven years of age he was a foot taller than his contemporaries, and weighed 168 pounds (normal average, 72 pounds). At twelve years his external characters of sex were those of an adult, but he has never shown any sexual instincts; no priapism or pollutions.

He was sent to a strict military academy, where in the course of a year an attempt was made to reduce his weight by excessive physical exercises. His parents and teachers attributed his condition to overeating; and, being much abused and teased by his schoolmates as a "stupid fat boy," he became depressed and melancholy. Though kept at school, there has been but little mental advance in the past two years; he shows no initiative faculties, "behaving in many respects like a boy of six."

Polyuria and polyphagia, with an abnormal appetite for sweets, extensive drowsiness, constipation, and sensitiveness to cold, have been marked features. Occasional attacks of vomiting have been attributed to overfeeding. There has been no headache.

Physical Examination. Practically negative except for the psychic conditions and signs attributed to disorder of internal secretion. Temperature markedly subnormal, often 97° . Pulse slow, often 60. Blood pressure variable, often below 100.



FIGS. 5 and 6.—Case III. Overgrowth, with adiposity. Height of patient on left, aged sixteen years, contrasted with that of father.

Mental Status. Memory poor; feeble powers of initiation and concentration; inattentive, irritable, morose. Speech hesitating, stuttering, and disconnected; responses slow, frequently irrelevant.

He falls asleep at any and every opportunity. Occasional involuntary twitchings of face and hands. He has a peculiar mania for writing inconsequential letters to people. *Neurologic examination* otherwise practically negative. No general pressure symptoms, though the optic disks are slightly congested. Pupils are irregular, with sluggish reactions and a coarse horizontal nystagmus, more marked to the left. There is a peculiar ataxia in his gait, which may be of cerebellar origin.

Analysis of Hypophysial Symptoms. No neighborhood disturbances. The sella is of small size (0.8 by 0.7 cm.), but shows no abnormalities; sphenoidal cells unusually large and extend into the dorsum sellæ.

Skeletal Configuration. Height, 173.5 cm. (5 feet 8 $\frac{1}{4}$ inches, or 3 $\frac{1}{4}$ inches above the average), despite a marked dorsal kyphosis. Usually large frontal sinuses, but otherwise no cranial abnormalities; circumference, 56.5 cm. Eyes deeply set; dental arches narrow; second teeth small but well formed. Limbs long and tapering. Extremities large; wears an 8 $\frac{1}{2}$ shoe. Circumference of thorax, 98 cm.; of hips, 102 cm. There is a suggestion of *typus femininus*; slight genu valgum (Figs. 5 and 6).

Cutaneous. Skin is soft and dry. Extremities dusky and cyanotic. Many purplish lineæ atrophicæ. Definite hypertrichosis. Hair abundant in zone around upper sacral level, over extremities, pubes, and axillæ. Pubic growth since twelve years of age. There is some hair on chin and lips; has shaved at intervals for the past year. Eyebrows heavy.

Adiposity marked, with considerable tenderness on pressure. At eleven years patient weighed 168 pounds; present weight, 178 pounds (Boas gives the average as 110). Special accumulations of fat over abdomen, hips, pectoral regions, and inner aspect of thighs.

Metabolic activity low (*cf.* polyphagia, adiposity, subnormal temperature, etc.). Levulose assimilation limit, 250 grams.

Other Ductless Glands. Thyroid small; isthmus barely palpable. Thymus, pancreas, and adrenals negative. Testes normal; scrotum lax. Penis undeveloped (*cf.* early acquirement of secondary characters without development of sexual instinct).

June 10. Discharged, taking pituitary tablets.

Though these patients exhibit a syndrome of adiposogenital dystrophy, it is apparent that in some essential features they fail to conform with the type of Fröhlich.

Doubtless these disturbances of growth and metabolism would never have been credited with any possible alliance with a ductless gland disorder, and particularly with an hypophysial disorder, were it not for the fact that corresponding syndromes occur when the gland's activity has obviously been implicated in one way or another in association with a gross lesion of the neighborhood.

Fortunately, both in maladies associated with skeletal overgrowth or dwarfism and in those accompanied by excessive adiposity with genital derangement, pituitary hypertrophies, tumors or cysts, have been found often enough to justify us in attributing similar clinical pictures to a corresponding secretory change in the absence of a local neoplasm.

In varying grades the type is doubtless a common one, more or less familiar to all. One need but recall the fat boy depicted in "The Pickwick Papers," whose employment with Mr. Wardle consisted in alternate eating and sleeping. The combination of drowsiness, inertia, and an excessive appetite is often merely an expression of metabolic inactivity due to ductless gland insufficiencies.

CONCLUSION. The view is advanced that skeletal overgrowth, possibly combined with certain cutaneous changes and hypertrichosis, is an indication of anterior lobe hyperplasia. On the other hand, certain types of adiposity with an increased assimilation limit for carbohydrates, often with dry skin, subnormal temperature and pulse, are characteristic of the metabolic disturbances from posterior lobe insufficiencies. Hypotrichosis and sexual dystrophy are common accompaniments.

Assuming the combination of these factors, certain not unfamiliar clinical syndromes, in which overgrowth is associated with adiposogenital dystrophy, can be explained. They differ from the accepted syndrome of Fröhlich not only in the absence of an hypophyseal tumor with sellar enlargement, but also in their opposed skeletal features.

These physical states, in brief, are interpreted as the expression of an anterior lobe hyperplasia combined either with posterior lobe hypoplasia or with what is in effect the same thing, stasis of posterior lobe secretion.

GASTRIC DISTURBANCES IN TABES DORSALIS.

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DURING the past year the writer has observed five patients who presented themselves because of gastric disturbance, in whom this ultimately proved to be but one of the manifestations of tabes dorsalis. None of these patients had previously been made aware of the real nature of their disease, though all had been suffering for years. Two had been operated upon for supposed gastric ulcer, without the slightest relief of their symptoms; and a third was also subjected to surgery, by the advice of the writer, before

the fact was discovered that no organic disease of the stomach existed and the real situation was disclosed. All these facts seem to indicate that the gastric manifestations of tabes are not always recognized as promptly as they might be, and that perhaps more cases of "stomach trouble" are in fact spinal in origin than is generally realized.

The first case to be reported is a particularly remarkable one because of the unusual association of hematemesis with the gastric crises.

CASE I.—T. Y., a Japanese, aged thirty-four years, was first seen in September, 1911, complaining of stomach trouble.

History: For seven years he had had recurring attacks of abdominal pain, with vomiting. These came at irregular intervals. Between times he felt perfectly well. During 1910 he had two severe attacks. In 1911 the last one came about five weeks before we saw him first, and he had then been in the hospital for three weeks. Previously to that he had been at work and feeling well.

The pain was always felt in the pit of the stomach; did not radiate from there; was very severe; in character was described as a "shooting pain;" came on without reference to food taken; frequently began in the night, arousing him from sleep; lasted for several days without relief. Vomiting was constant while the pain lasted, but did not give relief. Taking food made no difference one way or the other, but no food was retained or desired. With his last attack he had vomited blood, but never before.

Physical Examination: The patient was a well nourished man, apparently well. No abnormality was found in heart, lungs, liver, or spleen. The abdomen showed slightly greater fulness and rigidity in the left hypochondrium than in the right, but no tenderness over the stomach; no palpable mass; no succussion splash; no peristaltic wave; no evidence of dilatation or of pyloric obstruction. The patient pointed always to the lower end of the ensiform as the site of his pain.

Gastric Analysis: One hour after the Ewald test meal four ounces of contents were removed, not well triturated, showing a little blood, much thick, ropy mucus, a few chunks of meat, and considerable butter, retained from the previous meal six hours before. Total acidity, 48; free HCl, 16; combined HCl, 16; organic acids and acid salts, 16.

TREATMENT. The patient was advised as to his diet, excluding all coarse and irritating foods, but was given no medicine. He remained perfectly well for two months following.

Recurrence: On November 29 he returned to Lane Hospital, because the previous afternoon he began suddenly and without warning to have violent pain in his stomach, and to vomit blood. In spite of withholding all food by mouth, applying an ice-bag over the stomach, and giving morphine hypodermically, he con-

tinued during November 29 and 30 to have violent pain and to vomit repeatedly, the vomitus being a brownish, bloody fluid, containing numerous shreds and flecks of brownish or reddish material which responded to all tests for blood. After two days the vomiting and pain suddenly ceased, and he was able to take food.

OPERATION. Convinced after witnessing this attack that there must be some serious organic disease of the stomach, most probably ulcer, we advised exploratory laparotomy. This was done by Dr. Stanley Stillman on December 9, but no abnormality of any kind was found in stomach, duodenum, gall-bladder, liver, or appendix, and the abdomen was closed without anything done but exploration. Except for another violent attack of pain and vomiting, with the same character of bloody vomitus as before, shortly following the operation, the convalescence was uneventful.

Further Recurrence: On April 16, 1912, the patient was again brought to Lanc Hospital from his home in the country. Following his operation he remained well and gained in weight. On the evening of April 15 he began again to have a violent paroxysm of pain and vomiting, vomited all night, and the same bloody material as before. Seen at 9 A.M. on April 16, he was retching violently, and had brought up in repeated small amounts about eight ounces of a dark brownish material, with much mucus, plainly bloody. He continued to have pain and hematemesis for three days, when the attack abruptly ceased.

Spinal Fluid: On April 19, 5 c.c. of spinal fluid were obtained by lumbar puncture. This showed a faint opalescence on boiling; positive Nonne reaction; negative Noguchii; sixty lymphocytes in 1 c.mm., and no polymorphonuclears; a positive Wassermann reaction in all dilutions.

Evidence of Tabes. Further physical examination now elicited the following facts:

Pupils: The right was regular in outline, the left was slightly irregular, and both reacted incompletely and sluggishly to light.

Abdominal reflex was present and lively on both sides, likewise the cremasteric.

The plantar, achilles, and patellar reflexes were completely missing on both sides.

Sensation was diminished over the legs from the knees down to heat and cold and to pain, but not to touch; the patient swayed when standing with eyes closed, and had to be supported or he would have fallen; he walked clumsily and stumbled, but his gait was not definitely ataxic.

Subsequent History: On April 29 the patient was given 0.6 gram of salvarsan intravenously, and a prescription containing bichloride of mercury and iodide of potassium for regular use by mouth. In spite of this treatment he had another attack in May

and another in June; he then returned to Japan, and we have had no further report of his condition.

A case similar to this forms the subject of one of Charcot's lectures in his *Leçons du Mardi*.¹ He speaks of hematemesis, "vomissements noirs," as a rare feature in gastric crises, and says that besides this case of the patient he is presenting he knew of but one other, previously reported by Vulpian. But that was in 1889. Oppenheim,² in the latest edition of his text-book on nervous diseases, mentions hematemesis as a rare occurrence in gastric crises, but refers to observations of it by Vulpian, Charcot, von Noorden, Eckert, Rubin, Neuman himself, and Von Jappa³ reports a case of gastric crises associated with hematemesis during one recent attack, but not with any other previous, though they had recurred at intervals for six years. At autopsy this patient was found to have not only characteristic spinal changes, but in the stomach the scar of a gastric ulcer, with an eroded vessel. Von Jappa questions whether in such a case the gastric ulcer is simple accidental coincidence or is a mucous membrane defect secondary to trophic disturbance from tabes. He agrees that it is possible to have pure parenchymatous bleeding in gastric crises, without ulcer, and such was the condition in the case of the Japanese just reported, for the stomach was examined carefully at the operation and no ulcer was found. Ranzier and Roger⁴ have also recorded the history of a case of severe gastric crises, ultimately accompanied by hematemesis, and closely resembling gastric ulcer. Probably as more such cases are put on record, and attention is called to the possibility, the correct interpretation will more frequently be made previous to laparotomy.

CASE II.—A Scotchman, aged forty-one years, was first seen in the medical ward of Lane Hospital in October, 1911. He complained of attacks of pain in the pit of the stomach, with nausea and vomiting, recurring for two and a half years past; though he had had "stomach trouble"—sour eructations and belching after eating—for ten or twelve years before that. His severe attacks were frequent, with only a few days intermission, and they lasted only for one day or sometimes for three or four. They seemed to have no relation to the taking of food. They came on suddenly, with sharp, cutting pain in the pit of the stomach, nausea, and repeated vomiting. He had never vomited any blood nor passed any by bowel. Three months before coming to the hospital he had had his abdomen opened, but was told that nothing was found, and his attacks persisted afterward as before.

¹ Charcot, *Oeuvres Complètes*, ii, 331.

² Fünfte Auflage, S. 174.

³ Ueber Bluterbrechen bei gastrischen Krisen, Inaug. Dissert., Berlin, 1911.

⁴ Crises gastriques subintrantes avec hematemesis au cours d'un tabes fruste, Montpellier Méd., 1911, No. 41.

This patient was found⁵ to have inequality of his pupils, the right being markedly larger than the left; neither pupil reacted to light, and the left only slightly to accommodation, the right not at all. The left Achilles tendon reflex was absent, but the right was lively; the corneal reflex was absent in both eyes; but all other superficial and deep reflexes were normal. Hyperesthesia to heat and cold, with hypesthesia to tactile irritation, was found over both lower limbs from knees to hips, and continuing over the trunk posteriorly as high as the angles of the scapulæ, but extending anteriorly only as far forward as the nipple line on each side, leaving the abdominal wall above Poupart's ligaments apparently normal in its sensibility.

There was a positive Wassermann reaction in the blood and in the spinal fluid, and the latter showed 20 cells per cubic millimeter, all lymphocytes. The stomach showed hypersecretion not only after the Ewald meal but also in the fasting state, in the early morning.

This patient twice received salvarsan intravenously, with the result that his gastric crises occurred much farther apart afterward, and were briefer in duration, but they did not entirely cease.

CASE III.—A Japanese, aged twenty-eight years, entered the medical ward at Lane Hospital in January, 1912, complaining of stomach trouble. During the year and a half previous he had had four or five similar attacks. The present attack began four weeks before. The characteristic feature of this case was vomiting; at the outset he vomited for four or five days every fifteen minutes without stopping, then for two days he did not vomit at all; since then he had vomited several days at a time quite frequently, with intervals of several days with none. He also complained of pain, burning in character, up and down the anterior surface of the trunk, from throat to navel, present continuously for five weeks. No previous attack had ever lasted over two weeks.

This patient showed loss of both patellar and both Achilles reflexes, but no other evidences of tabes. His blood and spinal fluid both showed positive Wassermann reaction, and the spinal fluid contained 26 lymphocytes per cubic millimeter.

After salvarsan intravenously his condition was much improved, and his vomiting and pain gradually ceased, but his subsequent course could not be followed.

Duration of Gastric Crises. The two cases just described bring up the question of possible duration and frequency of gastric crises in tabes. The ordinary course is that noted in Case I. Attacks come at intervals of two or three months and last for three days to a week, repeating themselves throughout three to

⁵ In the neurological examination of this and of the subsequent cases I have had the coöperation of Dr. W. F. Schaller, instructor in neurology in Stanford University, Medical Department.

six years. But Charcot, in his description of the possible variations from type, mentions gastric crises that occur with great frequency, even daily, but lasting for only four or five hours; while, on the other hand, the length of the crisis, in place of three, four, or five days, as in the typical condition, may be extended to fifteen or twenty days, a month, or even more, while at the same time the intervals shorten. Thus the gastric disturbances of tabes may even establish themselves as more or less of a permanency, without cessation or intermission, for a period of many months.

CASE IV.—An Irish laborer, aged forty-seven years, was first seen in October, 1908, complaining of stomach trouble. For six or seven years before he had had recurring attacks of the same sort, at first with several months' interval, but gradually growing more frequent. They were characterized by nausea, belching, vomiting, but no intense pain, only a gnawing, distressed feeling. Such attacks always lasted only a week or two, and in the interval he always felt well. During an attack all food increased his distress, and he feared to eat. Vomiting came on because of the discomfort, and usually relieved it. He had never vomited any blood. The present attack, that brought him for advice, was the most severe he had ever had. His stomach was found dilated, but there was no palpable tumor over it and no tenderness. The contents gave a total acidity of 100 and free HCl 60. The case was only seen for diagnosis at that time, and was not understood, though ulcer was suspected.

The man was not seen again until August, 1912, when he returned for advice about pains in his chest. Subsequent to his previous visit he had no further attack of his stomach trouble for two years, and then only a mild recurrence, and after that no more at all. In February, 1912, he began to have dull pain in his lower limbs, from his knees down, like rheumatism, but could stand or walk without increase of pain. Suddenly the pain left his lower limbs and went up into his abdomen and back; it was felt around the trunk, particularly over the abdomen, but less severely in the back; the abdomen was tender to touch, he said, in the region where he felt his pain. Since this pain began he had lost twenty to thirty pounds in weight, and had become so weak he could hardly move around. Examination showed that over the back, between the sixth and tenth thoracic vertebræ, he had a definite area of hyperesthesia to touch or pressure, but not to pin-prick or heat or cold; evidently due to an inflammation of meninges and nerve roots in his lower dorsal region. In his lower limbs from feet to knees he also showed a disturbance of sensation, inability to distinguish heat from cold, and pin-head from pin-point. The right pupil was smaller than the left, fixed, and did not react to light; the left reacted to light, but sluggishly. There was no loss of plantar or patellar reflexes, but the Achilles was less on the right

than on the left side. The blood and the spinal fluid both gave a positive Wassermann reaction, while the spinal fluid showed also a positive Nonne and a positive Noguchi reaction, and 20 cells to the cubic millimeter.

This case brings out several points long ago emphasized by Chareot and since by others, but apparently not yet thoroughly appreciated in diagnostic work. (1) The gastric crises of tabes occur most often in that early period of the malady before motor ataxia has yet appeared, the pre-ataxie period. This phase may continue for years before locomotor troubles show themselves, and during this time the crises may be the sole manifestation of the spinal disease. This absence of other recognized symptoms of tabes in association with the gastric attacks no doubt often misleads the physician and makes him fail to understand the real nature of the condition. But even during this pre-ataxie stage there may be minor signs of whose existence the patient is totally unaware, such as slight inequality of the pupils or a fixed pupil that does not react to light, or an absent reflex in knee or Achilles tendon, or an area of disturbed cutaneous sensation. Lumbar puncture and spinal fluid also now afford valuable aids to diagnosis, even in the pre-ataxie stage. (2) As the other symptoms of locomotor ataxia appear and progress, the gastric crises are likely to cease spontaneously, and after having suffered from them for years, the patient may finally be freed from them entirely, as the evidences of ataxia and motor incoördination appear upon the scene. (3) There are incomplete and atypical gastric crises, "formes frustes," as Chareot called them, of which this case forms an example, for the usual violent pain was lacking from his attacks. In another case it may be the vomiting that is lacking, while pain in the epigastrium is acute and prostrating. Other possible deviations from the usual type, as regards frequency of repetition of the attacks and as regards duration, have been mentioned in commenting on Cases II and III.

CASE V.—K. M., a Japanese, was first seen in July 1912, complaining of stomach trouble. About seven years before he commenced to have attacks of severe pain in the stomach, but without vomiting. Six years before he had been operated upon in the country, the abdomen opened, and the stomach explored. He did not know what was found, but his attacks continued after the operation just the same. Later on these attacks consisted of vomiting and diarrhea as well as of pain. Such attacks lasted for three or four days, he said, and recurred irregularly every few months. The one observed in July, 1912, included very violent epigastric pain, repeated and violent retching, inability to retain any nourishment, many bowel movements each day, apparently without cramps, considerable prostration; the whole illness lasted four days; he said there had been none before for five months. He

recovered from it quite suddenly, and after it ceased was at once hungry and able to eat. The stomach was not dilated nor tender nor abnormal in contour. The contents showed no free or combined HCl, and a total acidity of but 16. The right patellar reflex was much less active than the left; the left Achilles reflex was absent entirely; there was no abnormality of the pupils. The spinal fluid showed 14 cells per cubic millimeter and a positive Wassermann reaction.

It seems remarkable that 3 out of these 5 patients observed have been Japanese. They constitute a small proportion of our material in San Francisco, and the frequency in this race of gastric crises as well as of other manifestations of tabes and of syphilis of the nervous system makes us suspect that they must be inadequately treated in their own country at the time of their initial infection.

SUMMARY. The recognition that certain gastric disturbances are really due to tabes is never difficult if one is alert to the possibility. There is no fixed unchangeable rule about the nature of these disturbances, or about their duration, or their frequency of recurrence, to make their diagnosis easy. They are not accompanied by the evidences of organic disease in the stomach that one expects to find; they recur in spite of treatment of all kinds directed to the stomach, even in spite of laparotomy; they usually appear abruptly, without reason, and cease suddenly regardless of treatment, leaving the patient perfectly free from gastric disturbance in the intervals. On the other hand, no manifestations of "locomotor ataxia" may be present for years during which the stomach upsets continue, and the patient may make none of the complaints that one expects to hear when spinal disease exists. The proof of the connection between the gastric disturbance and the spinal lesion, therefore, must often depend upon the discovery of signs of tabes of which the patient is unaware—such as faulty reflexes and cutaneous sensibility, and changes in the spinal fluid obtained by lumbar puncture; while the demonstration that active syphilis exists, by the Wassermann reaction in the blood and spinal fluid or even in the latter alone, adds the last link to the chain.

THE LYMPHOCYTOSIS OF INFECTION.

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THE great majority of infectious diseases are accompanied during their acute stages by increase in the polynuclear leukocytes. A few, like typhoid and malaria, show no marked change

of any kind. *Occasionally infections usually associated with polynuclear leukocytosis show instead an increase of lymphocytes.* This was noticed many years ago by Ehrlich, and attributed by him to a passive drifting of lymphocytes out of the lymph glands and contrasted with the active emigration of the polynuclear leukocytes. Most writers have not agreed with this interpretation, but a number have noticed the occurrence of the phenomenon to be explained. It is most striking and has been most often commented upon in connection with whooping cough, where it is so constant as to be believed by some to be of value in differential diagnosis of that disease.

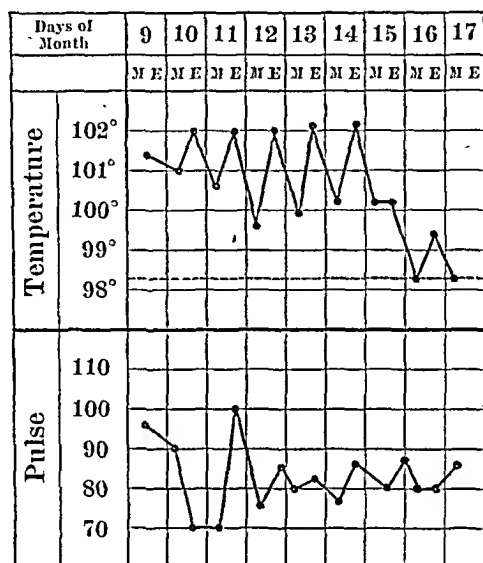
The group of cases to which I wish to call attention are such as would ordinarily be associated with polynuclear leukocytosis. They appear to be connected, at least in some cases, with a streptococcal infection, and their practical interest to clinicians arises from the fact that they are liable to be confused with lymphatic leukemia and thus to cause an unnecessary alarm as to the prognosis.

CASE I.—Wound infection at autopsy; lymphangitis and adenitis; lymphocytosis; continued fever; recovery. About fifteen years ago a young physician acquired a hang-nail infection at an autopsy, the nature of which I do not know. This was followed by a mild lymphangitis extending up the arm, with enlargement of the axillary glands both on the corresponding side and to a lesser extent in the other axilla. There was continued fever for several weeks, with marked prostration, the case somewhat resembling typhoid fever. The blood showed throughout a well-marked absolute and relative lymphocytosis, such that the physician himself and other consultants were seriously alarmed as to the possibility of lymphatic leukemia. The record of blood counts was unfortunately not kept, but if my memory serves me the percentage of lymphocytes never rose above 70 and the total count of leukocytes never above 20,000. The lymphocytes were mostly of the smaller types, and there were no other changes in the blood. Recovery was rather slow, but complete. This physician has had no such attack since that time, and has remained in good health.

CASE II.—Boils; persistent lymphocytosis; recovery. A college undergraduate, aged twenty years, was seen November 15, 1909, on account of persistent boils, which had been present for six weeks. At the start of the illness there was said to have been bile in the urine and a slight yellowish discoloration of the conjunctivæ. He had been considerably run down at the time of the onset of these symptoms, losing much sleep and working very hard.

When I saw him he was already considerably better, but still had one or two large boils freely discharging. The chart for part of the week preceding and following the time when I saw him is subjoined herewith. November 15 his blood showed: red cells,

5,180,000; white cells, 3,400. Differential count showed polynuclears 18 per cent., lymphocytes of various types 82 per cent. One of the lymphocytes was in karyokinesis, and several showed nuclei in various stages of division. Most of the lymphocytes were small, but some had the characteristics of Türk's "stimulation forms."



Temperature chart of Case II.

November 16 the polynuclears were 21, lymphocytes 79.

November 19 the total leukocytes were 16,400, polynuclears 14 per cent., lymphocytes 86 per cent. In the meantime the boy was rapidly recovering, and showed practically no symptoms.

November 20 the differential count still showed polynuclears 14 per cent., lymphocytes 86 per cent., with an increase in the total number of leukocytes estimated at 15,000.

November 23 he went home for his vacation, and after his return, December 1, was perfectly well.

CASE III.—In the middle of a raging epidemic of streptococcic sore throats during January, 1912, a girl, aged twenty years, began to have a disagreeable morning headache. A week later lumps appeared under the right arm. A week later, February 3, she began to have a severe sore throat, with a temperature of 102°, lasting about four days, and accompanied by swellings in each side of the neck. During the following two weeks she had frequent night sweats. The swelling of the glands in the axilla continued and a gland became enlarged under the chin. After the fever left her she began to cough and continued to do so for three weeks, the sputum being sometimes slightly blood-streaked. With the decline of acute symptoms she continued to lose weight, strength, and color, and had a good deal of digestive disturbance.

February 16 her cervical glands, both lateral and posterior, were enlarged to the size of marbles, and in the right axilla there was a gland the size of a small hen's egg, with smaller ones in the left axilla. Glands in both groins were also demonstrably larger than the average. The spleen and liver were not felt; chest and abdomen negative, except for an abnormally dull percussion note in both apices, especially the right, and over the upper part of the sternum. The glands showed no signs of breaking down. The blood showed: total leukocytes 9000. Of these there were polynuclears 28 per cent., lymphocytes 71 per cent., eosinophiles 1 per cent.

She was seen again February 23, and was, on the whole, much better. The fever and sweating had altogether ceased, and all the glands were smaller, but still abnormal. The blood at this time showed: red cells, 5,600,000; white cells, 3600; of which there were polynuclears 36 per cent., lymphocytes 62 per cent., mast cells 2 per cent. She made an uninterrupted recovery from that time on.

CASE IV.—A man, aged thirty-seven years, had what he called "a cold" in February, 1912.

March 9 he had a severe attack of vertigo while in a barber's chair, but recovered in a few minutes and has had no more such attacks since. A certain amount of cough left over from his cold bothered him a good deal during March.

March 18 he awoke with glands in the left side of his neck, sore and swollen. After three days these glands subsided, but he began to have fever which on March 22 reached 101°. For the next ten days he was in bed, with slight evening fever and night sweats.

March 28. The blood examined by the attending physician showed 30,500 leukocytes, and the counts thereafter were as follows:

		Polynuclear.	Large lympho- cytes.	Small lympho- cytes.	Eosinophiles.
March 28	. . . 30,500	25 per cent.	67 per cent.	8 per cent.	
April 5	. . . 18,900	28 per cent.	58 per cent.	20 per cent.	
April 12	. . . 26,800	50 per cent.	8½ per cent.	41½ per cent.	½ per cent.
April 15	. . . 12,500	65 per cent.			
April 20	. . . 26,700	60 per cent.	15 per cent.	24 per cent.	¼ per cent.
April 27	. . . 14,500	51 per cent.	6 per cent.	41 per cent.	1⅓ per cent.
May 4	. . . 19,400	55 per cent.	13 per cent.	30 per cent.	2 per cent.
May 11	. . . 15,400	56 per cent.	4 per cent.	38 per cent.	1½ per cent.
May 18	. . . 18,800	57 per cent.	7 per cent.	35 per cent.	½ per cent.

I first saw the patient May 23. At that time he was much better, but the glands were still slightly enlarged in his neck. He had no more fever and was free from night sweats, although his cough continued to some extent in the morning, and unless he stayed out of doors most of the day his temperature in the afternoon rose to 99.5° or less. Physical examination on May 23 was negative. The white cells were then 8200, polynuclears 56

per cent., lymphocytes 42 per cent.; of these 38 per cent. were of the small type, eosinophils 2 per cent. His recovery thereafter was uneventful.

In the differential diagnosis between streptococcic adenitis, tuberculous adenitis, and lymphoid leukemia the most important point is the evidence of a cause for the adenitis, the course of the disease, and the percentage of lymphocytes in the differential count. Although this percentage is obviously much elevated, both absolutely and relatively in the cases reported here, it is considerably lower than the percentages usually seen in cases of lymphoid leukemia at that period of disease in which the patients feel sick enough to consult a physician. The majority of leukemic cases have over 90 per cent. of lymphocytes, and show in addition to the relatively well-formed cells many broken and partially decolorized remnants of leukocytes. I saw none of these broken cells in any of the cases above described.

In Case III, tuberculosis (pulmonary and glandular) had to be considered, on account of the three weeks' cough, the blood-streaked sputa, the fever, night sweats, loss of weight, and dullness at the pulmonary apices. Only by the course of the disease could tuberculosis be excluded, though the sudden onset of the symptoms in the midst of an epidemic of streptococcic sore throats made the balance incline toward septic rather than tuberculous infection.

It should be noted, moreover, that acute lymphoid leukemia often begins with symptoms like those present in Case III, and is sometimes associated with sore throat due to leukemic infiltration of the tonsillar ring.

In connection with the second of these cases I should like to call attention to the fact that an adenitis apparently originating in tonsillar infection, involved not only the cervical but axillary glands. In other such cases I have known suppuration in an axillary gland and isolation of pyogenic streptococci from the pus.

In 3 of the 4 cases here reported there is reason to believe that a streptococcus was the infecting agent. The fourth may have been of similar origin though no cultures were taken.

SUMMARY. 1. Wound sepsis, boils, and widespread streptococcic adenitis of tonsillar origin may be accompanied by a lymphocytosis so pronounced as to suggest lymphoid leukemia.

2. No reason is known for this substitution of lymphocytosis for the usual polynuclear leukocytosis of infection.

3. The distinction between such a lymphocytosis (accompanying a widespread adenitis) and leukemia depends upon the recognition of an infectious origin for the adenitis, upon the lesser degree of lymphocytosis in the infectious type, and upon the course of the disease.

GASTRIC ULCER WITHOUT FOOD RETENTION: A CLINICAL ANALYSIS OF ONE HUNDRED AND FORTY OPERATIVELY DEMONSTRATED CASES.

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To July 1, 1912, there had been 1341 operations performed for ulcer of the stomach and duodenum at the Mayo Clinic. Of this number, 404 were proved to be ulcers of the stomach. In 264 (65.3 per cent.) of these gastric ulcers there was definite food retention demonstrable after twelve hours by the raisin and cooked-rice test (Strauss, Hansmann). In 140 (34.6 per cent.) of these operatively proved gastric ulcers no food retention was evident.

The diagnosis of surgical gastric and duodenal ulcer *with* food retention is comparatively simple, but the recognition of gastric ulcer when the stomach's emptying power is still unimpaired offers much greater difficulties. While careful development of the history, routine physical examination, and scrutiny of test-meal and laboratory data frequently admit of tentative diagnosis of gastric ulcer, a large number of cases present a picture so blurred by duodenal, gall-bladder, and appendix manifestations that unreserved diagnosis is rare.

This report has been made in the endeavor to determine the possibility of exact prelaparotomy diagnosis of the above-mentioned group of cases.

Material. The analysis covers 140 cases of proved gastric ulcers, without food retention, from the services of W. J. and C. H. Mayo.

Age. Table I indicates that the largest number occurred between thirty and forty years of age (27.2 per cent.); 92 per cent. of all cases were between the ages of thirty and sixty.

TABLE I.

Age.	No. of cases.	Per cent.
0 to 10	0	0.0
10 to 20	0	0.0
20 to 30	21	15.0
30 to 40	38	27.2
40 to 50	31	22.2
50 to 60	39	28.0
60 to 70	8	5.1
Over 70	3	2.1

Sex. In this series there were 103 males (73.6 per cent) and 37 females (22.4 per cent.), or approximately 3 males to each female. Table II shows the number of each sex at different decades; 57 per cent. of the ulcers in women were between the ages of forty and sixty. In these two decades occurred 47+ per cent. of the ulcers in males. No case occurred in females after the sixth decade.

TABLE II.

Years.	Males.	Females.	Total.
0 to 10			
10 to 20			
20 to 30	14	7	21
30 to 40	29	9	38
40 to 50	25	6	31
50 to 60	24	15	39
60 to 70	8	0	8
Over 70	3	0	3

Nationality. American-born furnished 98 cases. The remainder were largely Swedish, Irish, and Canadian.

Occupation. A widely diversified range of occupation was exhibited. In the list were 46 farmers (32 per cent.), 5 physicians, 2 stonecutters, 2 blacksmiths, 2 miners, 1 brickmaker.

Habits. The histories indicate that ulcers occurred in 46 (32 per cent.) individuals using alcohol. In 10 there were evidences of its excessive use; 5 of the cases were heavy smokers.

Dietetic Errors. No definite data with respect to this feature is available. The occupational statistics may be suggestive.

Previous Infectious Diseases. A history of typhoid fever was obtained in 26 (18.9 per cent.). Pneumonia was noted in 6, scarlet fever in 8, measles in 8, syphilis in 5, gonorrhea in 6, la grippe (severe) in 4, rheumatism in 3, diphtheria in 2, smallpox in 2, malaria in 8.

In 2 cases there was nephritis; in 1 cirrhosis of the liver.

12 (8.5 per cent.) had previously been operated upon for appendicitis, and 2 for gallstones. These figures are instructive taken into consideration with the extragastric operative findings (*vide infra*).

Anemia. Where specifically noted the hemoglobin averaged 72 per cent. (Dare).

Nutrition. In 97 of the 140 cases definite figures were available respecting weight loss. The average loss was 20.5 pounds; the minimum loss was 5 pounds, the maximum 65 pounds. The rate of loss varied. In some cases patients were not aware of loss until weighed in the examining room. Other patients had lost weight rapidly, for example, 65 pounds in six months, 30 pounds in six weeks, 25 pounds in six weeks, 20 pounds in five weeks, 25 pounds in three weeks, etc. Even rapid weight loss was rarely associated with cachexia usually evident in malignant disease. Night pain with loss of sleep, constant pain with fear of aggravation on eating, or caution in diet on account of recent hemorrhage were prominent factors associated with rapid weight loss.

12 cases showed progressive gain in weight; 21 had neither lost nor gained.

Appetite. In 52 the appetite was noted "poor," in 52 "fair," in 36 "good." Frequently the appetite is lost in acute attacks of pain or distress. The dread of bringing on distress by food

ingestion sometimes causes a poor appetite habit. The same may be said of persistent "dieting."

Bowels. In 26 the bowel movements were "regular," in 12 "sluggish," in 92 (65+ per cent.) "constipated." In 10 there was diarrhea.

Character of Complaint. 104 (74.2 per cent.) gave histories of discomfort intermittently ("attacks," "spells," etc.). In 36 (26.6 per cent.) instances the ailment was continuous. In many cases there was an early history of "attacks," with recent change to continuous discomfort, frequently associated with weight and strength loss. The "attacks" were variously stated as three to five years, two to three years, or two to six months or two to five weeks apart. They were often noted as lasting a few hours or days to two to six months, irrespective of medical or other treatment. The attacks frequently bore relation to the seasons—spring and fall being favorites.

Previous Disorders of "Digestion." 81 per cent. of the cases came with a diagnosis, frequently self-given, of "dyspepsia" or "indigestion," usually "chronic." Table III furnishes significant and etiologic information (not altogether useless diagnostically) respecting this class of cases.

TABLE III.—Duration of Symptoms.

Years.	No. of cases.	Per cent.
Less than 1	8	5.7
1 to 5	30	21.4
5 to 10	32	22.8
10 to 15	29	20.7
15 to 20	14	10.0
20 to 25	9	6.4
25 to 30	7	5.0
Over 30	11	7.8

The table makes apparent that nearly 54 per cent. of the patients had been affected with disorders of "digestion" for from five to twenty years before operation; about 21 per cent. had been ill less than five years.

Age has only relative importance in the estimation of duration of an ulcerative process in the stomach. Frequently patients in the sixth decade of life have been perfectly well to within a few months of the disability that finally leads to operation (for example, six months, age fifty-eight years; five months, age fifty-three years; three months, age fifty-three years, etc.), while young adults give a history of from ten to twenty years of "indigestion."

SYMPTOMATOLOGY. 1. PAIN. Of the 140 proved ulcers without food retention in the series, pain is the one constant complaint.

(a) *Character of Abdominal Discomfort.* This was styled "distress" in 17, "burning feeling" in 21, "gnawing" in 25, "dull ache" in 33, severe ache in 13. In 31 there was history of colicky attacks ("cramps," "doubling up," tearing," etc.). In 18 instances (12.7 per cent.) these were severe enough to require hypodermic admin-

istrations of opiates. In 64 instances (45.7 per cent.) there were sensations of "upward pressure." In 17 (12.2 per cent.) pain or distress was continuous or appeared irregularly. In 27 instances (19.2 per cent.) night pain was a distressing feature.

(b) *Location, Symptomatically, of Abdominal Discomfort.* In 112 cases (80 per cent.) discomfort was said to be epigastric; in 29 epigastric to the rib edges (more often to the right); in 18 in the "pit of the stomach;" in 8 in the abdomen generally; in 2 in the "small of the back."

(c) *Transmission of Pain.* In 52 instances (37.1 per cent.) no transmission was given. In 25 cases pain was referred to the back (right side 22, left 3), usually below the tip of the scapula; in 25 cases to the rib edges (right 20, left 5); in 10 to the lower esophagus; in 7 to the infranavel region; in 7 to the shoulder-blades (right 5, left 2); in 3 each to navel, nipples, thorax generally, and "tip" of the sternum; in 2 to the throat.

(d) *Food Relation.* In 123 cases (87.8 per cent.) pain has a definite relation to ingestion of food. The summary in Table IV demonstrates the actual time relation of food and abdominal discomfort.

TABLE IV.

Time of pain in hours after eating.	No. of cases.	Per cent.
Immediately	4	2.8
Less than 1 hour	17	12.2
1 to 2 hours	22	15.7
2 to 3 hours	33	23.7
3 to 4 hours	34	24.7
4 to 5 hours	10	7.1
Over 5 hours and irregularly	20	14.0

Some overlapping is exhibited in Table IV, inasmuch as pain may vary as to time in the different attacks. It will be noted that in more than 79 per cent. of instances, pain appeared within four hours following the ingestion of food. The taking of food frequently temporarily relieved actual pain, as shown below.

(e) *Relation of Time to Pain or Distress to Location of Ulcer.*

TABLE V.

Location of ulcers.	Less than one hour, p. c.	One to two hours, p. c.	Two to three hours, p. c.	Three to four hours, p. c.	Four to five hours, p. c.	Over five hours, p. c.	Irregularly.	Total.	Per cent.	Night pain.
Pyloric	6	5	23	19	6	0	6	65	46.4	12
Prepyloric	0	1	1	3	1	0	0	5	3.5	0
Lesser curvature	5	10	13	7	3	1	4	43	30.7	14
Near cardia	4	2	1	2	0	0	0	9	6.4	0
Posterior wall	4	2	2	2	1	0	1	12	8.5	1
Anterior wall	0	0	1	1	0	0	0	2	1.4	0
Total	19	20	41	33	11	1	11	136		27

Unclassified, 4. Night pain cases not included in totals,

Table V demonstrates that irrespective of the location of the ulcer, 83 per cent. have pain or distress within four hours after eating, and more than 54 per cent. have pain or distress within two to four hours after eating. More than 64 per cent. of ulcers involving the pylorus have pain from two to four hours after eating; more than 53 per cent. of lesser curve ulcers have pain from one to three hours after eating; more than 66 per cent. of ulcers near the cardia have pain less than two hours after eating, more than 44 per cent. less than one hour after eating; more than 66 per cent. of ulcers on the posterior wall have pain within three hours after eating, and 33 per cent. have pain within one hour after eating.

(f) *Pain Control.* Except in acute attacks (for example "colics," perforation, etc.) gastric ulcer pain is usually eased or relieved by limitation of the amount and character of ingested food (diet), the taking of food when distress is marked (food-ease), the neutralization of acid by the alkalis, or by emptying the stomach (vomiting or lavage). As has been shown in this series, opiates were required in 12.7 per cent. of instances, usually in aggravated "spells."

Table VI demonstrates the relative value in our series of the various common pain controls. The tabulations may be so read as to show the relative frequency of relief from any combination of pain controls. The most common combination of controls proved to be diet, food ingestion, alkali, and vomiting.

TABLE VI.—Pain Control.

Type of control.	Total cases.	Food.	Vomiting.	Liquids.	Alkali.	Lavage.	Diet.	Rest.	Pressure.	Opiate.
Food	93	0	49	14	68	14	83	15	5	11
Vomiting	71	49	0	9	41	11	65	10	2	7
Liquids	16	14	9	0	13	4	14	1	2	0
Alkali	82	68	41	13	0	9	77	9	3	10
Lavage	15	14	11	4	9	0	12	1	0	0
Diet	121	83	10	1	9	1	0	12	1	13
Rest	20	15	10	1	9	1	12	0	1	3
Pressure	7	5	2	2	3	0	4	1	0	1
Opiate	18	11	7	0	10	0	13	3	1	0

Explanation: Read times each control gave distress relief in column "Total Cases." For combinations of pain controls read table up and down.

Table VII attempts to correlate these factors with respect to the locations of the ulcer demonstrated operatively.

(g) *Relation of Position of Ulcer to Pain Control.*

TABLE VII.

	Diet.	Food relief.	Alkali.	Vomit.
Pyloric	57	49	37	36
Prepyloric	0	0	0	0
Lesser curvature	51	37	38	26
Near cardia	3	2	1	2
Posterior wall	7	5	4	3
Anterior wall	4	3	3	1
	132	96	83	68

(h) *Areas of Abdominal Tenderness by Palpation.* Of the 140 proved ulcer cases, 126 (95 per cent.) exhibited epigastric tenderness. In 109 (77.8 per cent.) the tenderness was more marked to the right of the midline. In 17 (12 per cent.) the tenderness was prominent to the left of the midline. In 23 instances (16+ per cent.) there was special tenderness in the "pit" irrespective of general epigastric sensitiveness. In 20 instances (14+ per cent.) there was definite exaggeration of tenderness at the right rib border, distinct from widespread epigastric muscle spasm. Five patients (3+ per cent.) exhibited special left rib margin tenderness. In 5 cases (3+ per cent.) the area just above the navel was painful to pressure. On but 1 patient was no abdominal tenderness demonstrated. Ridges, invariably tender, were palpable four times.

(i) *Relation of Areas of Abdominal Tenderness to Location of Ulcer as Found at Operation.* Table V shows that of the 140 ulcers examined, practically half (49.9 per cent.) were pyloric or prepyloric, while more than four-fifths (80.6 per cent.) of the entire series were located at the pylorus and the pyloric half of the lesser curvature.

It has been shown above that in 95 per cent. of our cases here reported there was definite epigastric tenderness. While 46.4 per cent. of all the ulcers were located at the pylorus, in only 14+ per cent. was there increased tenderness toward the rib margin, that is, the anatomic situation of the pylorus. While 30.7 per cent. of all the ulcers were on the lesser curvature, but 16+ per cent. of the cases showed definite tenderness in the pit or midepigastrium.

We have also shown that symptomatically the patient's complaints of distress are in close harmony with the physical evidences of tenderness. In this classification 80 per cent. referred the pain to the epigastrium generally, 14 per cent. to the right costal arch region, and 12.8 per cent. to the pit. There were 8 (5.7 per cent.) ulcers located at or near the cardia. In more than twice that number there was noted high pit tenderness.

It would seem that only when taken with other observations are pain areas, symptomatically, or points of abdominal tenderness of value in definitely localizing ulceration of the stomach.

(j) *Relation of Evidences of Perforation of Gastric Ulcer to Actual Evidence of such as Demonstrated at Operation.* In our series, 46 cases (32.8 per cent.) had history and physical findings of acute or chronic perforation. In 24 cases (17+ per cent.) suggestion of perforation was possible. At operation 51 (36.4 per cent.) ulcers had perforated (9 acute, 3 subacute, 39 chronic). It would seem that only when history and physical findings of perforation are quite marked can one safely prognosticate an operative finding with fair degree of certainty.

2. VOMITING. (a) *Frequency.* This proved a prominent symptom. Of the 140 cases considered, 99 (70.7 per cent.) gave a history

of at some time vomiting sour fluid, food, or blood. Of the 99 cases, 65 vomited sour fluid alone, 24 vomited sour fluid and food. In the series 50 cases vomited but had no hematemesis, 31 vomited and also had hematemesis, 18 had hematemesis alone. Ten cases regularly *induced* vomiting of sour fluid and food to gain relief from pain.

Of the 99 vomiters, 39 vomited regularly. Eleven had "spells" of vomiting with vomit-free intervals of greater or less length, while 49 vomited only occasionally.

Nausea, Waterbrash, Eructations: In 12 cases, nausea without vomiting was a distressing symptom. "Waterbrash" with or without vomiting was prominent in 26 instances (19+ per cent.)

Pyrosis and eructations were noted in 123 (87.8 per cent.).

(b) *Time of Vomiting.* Of the 99 vomiters, in 35 (35.3 per cent.) the vomiting occurred when abdominal distress was most marked. In 28 instances (28 per cent.), ingestion of food precipitated vomiting. In 29 (29+ per cent.) vomiting was irregular. In 7 (5 per cent.) night vomiting was prominent.

(c) *Vomiting Relation to Food.* Table VIII summarizes this class of cases. It will be noted therein that more than 53 per cent. of these cases vomited within three hours following the taking of food.

TABLE VIII.—Relation to Food.

Time.	Number.
Less than 1 hour after eating	6
1 to 2 hours after eating	4
2 to 3 hours after eating	5
3 to 4 hours after eating	6
4 to 5 hours after eating	3
Over 5 hours after eating	4

(d) *Relation of Ulcer Position to Vomiting.* In Table IX we have summarized our experience in this respect with regard to the character of the vomitus and ulcer location. The most marked feature of the table is the numerical evidence supporting the clinical experience that ulcers at the pylorus and pyloric half of the lesser curvature are commonly associated with vomiting. This appears so especially when we recall that this series deals with gastric ulcer where the stomach emptying power has not been interfered with.

TABLE IX.—Relation of Vomiting to Location of Ulcer Found at Operation.

Location.	Blood alone.	Sour fluid and food without hematemesis.	Hematemesis, sour fluid and food.	Food.
Pyloric	10	23	17	9
Prepyloric	0	0	1	1
Lesser curvature	8	21	8	11
Near cardia	0	2	2	0
Posterior wall	0	3	2	2
Anterior wall	0	1	1	1
Totals	18	50	31	24

3. HEMORRHAGE. (a) *Frequency*. While clinically this sign has special emphasis placed upon it, of the 140 proved gastric ulcers analyzed herewith but 57 (40.7 per cent.) gave a history of bleeding. Of this number 47 (33.7 per cent.) had hematemesis, with or without melena; 25 had hematemesis alone; 32 (22.8 per cent.) had melena with or without hematemesis; 10 (7.1 per cent.) had melena alone; 22 (15+ per cent.) had both hematemesis and melena.

Number: The minimum number of hemorrhages was 1. The maximum 10.

(b) *Severity of Hemorrhage*. In 13 instances the patient experienced no particular inconvenience; in 21 there was faintness, while 23 patients actually fainted.

Amount of Blood Lost: This was given as varying from a "half-pint" to "a gallon."

(c) *Character of Hematemesis*. In 2 instances large clots were vomited. In the remaining cases the blood was fluid.

(d) *Relation of Ulcer Location to Hemorrhage*. Our experience is represented in Table X. It may be observed that irrespective of location of the ulcer, hematemesis alone is most common. It is also interesting to observe that melena may accompany an ulcer located anywhere in the wall of the stomach, and that this may occur without hematemesis in a considerable proportion of cases.

TABLE X.—Relation of Position of Ulcer to Hemorrhage.

Location.	Hematemesis alone.	Hematemesis and melena.	Melena alone.	Total hemorrhage each location.
Pyloric	10	12	4	26
Prepyloric	1	2	0	3
Lesser curvature	9	4	4	17
Near cardia	2	3	0	5
Posterior wall	3	1	1	5
Anterior wall	0	0	1	1
Totals	25	22	10	57

(e) *Relation of Hemorrhage to the Character of Ulcer Operatively Demonstrated*. Table XI details our findings. It is apparent that while all classes of ulcer bleed, yet nearly two-thirds (63+ per cent.) of those doing so show some grade of perforation at the laparotomy.

TABLE XI.—Relation of Hemorrhage to Character of Ulcer Found at Operation.

Character of ulcer.	No. of Cases.
Indurated ("calloused") ulcer	16
Acute perforating	6
Chronic perforating	8
Chronic indurated perforating ulcer with adhesions	17
Saddle ulcer	5
Saddle ulcer with adhesions	5
Total	57

4. **TEST-MEAL FINDINGS.** In the Mayo Clinic series (before mentioned) of operated gastric ulcers (404 cases), it will be recalled that 264 (65.3 per cent.) showed definite food retention by the tests of Strauss and Hansmann. In the remaining 140 cases, which comprise this analysis, 131 (93.7 per cent.) routine test-meal reports are available for tabulation. In 9 instances test-meals were not given, or if given only absence of food retention is noted.

(a) *Blood.* This was noted in 16 (12.2 per cent.) macroscopically or chemically by guaiac or benzdin tests.

(b) *Bile.* Twelve (9.2 per cent.) gastric extracts showed bile macroscopically or by chemical test (Goodel).

(c) *Lactic Acid* was demonstrated 4 times (3.1 per cent.) by the modified Uffelmann test.

(d) *Quantitative Estimation of Inorganic Acid.* The figures quoted are those obtained from filtered gastric extracts obtained about one hour following the Ewald breakfast, which had been preceded twelve hours by a full meal, including boiled rice and raisins.

Inasmuch as pyloric obstruction with food retention masks the true secretory picture in gastric ulcer, the tables compiled from our cases would appear to be especially suggestive.

Table XII details the quantitative estimation of total acidity and free hydrochloric acid by the Töpfer method.

Table XIII summarizes the amounts of "combined" hydrochloric acid.

TABLE XII.—Test-meal Acidities.

	0	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100
Total acidity	0	4	2	5	16	24	29	25	13	4	5	4
Free HCl	5	2	5	23	26	27	18	12	6	5	0	2
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
Totals	5	6	7	28	42	51	47	37	19	9	5	6

TABLE XIII.—Combined HCl.

	0	0-10	10-20	20-30	30-40	40-50
Combined HCl	4	26	83	17	1	0

Total Acidity: In 79.1 per cent of the cases this ranged between 35 and 75 with an average of 55.

Free HCl: More than 79 per cent. of meals showed free HCl of from 25 to 55, with an average of 42.5, irrespective of ulcer location (*Vide infra*).

"Combined" HCl: In more than 82 per cent. of instances this varied between 10 and 20. Only four times was "combined" HCl absent.

(e) *Relation of Total Acidity and Free HCl to Location of Ulcer Demonstrated Operatively.* The summary to Table XIV demonstrates that total acidity is quite noticeably higher in ulcers involv-

ing the lesser curvature than in those of any other location except on the anterior wall. The 2 cases tabulated in the latter position showed average total acidity of 70. It would seem that this number is too small on which to base conclusions.

TABLE XIV.—Relations of Total Acidity to Location of Ulcer Found at Operation.

Location . . .	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total
Pyloric . . .	0	1	0	9	11	11	15	8	4	3	1	63
Prepyloric . . .	1	0	1	1	1	1	0	0	0	0	0	5
Lesser curvature . . .	2	1	3	4	4	5	10	8	2	0	3	42
Near cardia . . .	0	0	1	0	2	3	2	0	0	0	0	8
Posterior wall . . .	1	0	0	0	4	4	2	0	0	0	0	11
Anterior wall . . .	0	0	0	0	0	1	0	0	1	0	0	2
Totals . . .	4	2	5	14	22	25	29	16	7	3	4	131

SUMMARY.

Average total acidity—pyloric ulcer	56.0
Average total acidity—lesser curvature ulcer	62.4
Average total acidity—ulcer at or near cardia	51.0
Average total acidity—ulcer posterior wall	48.7
Average total acidity—ulcer anterior wall	70.0

Table XV makes apparent that our material showed noticeably greater free HCl in ulcers at the pylorus than in any other class, except the two tabulated as being on the anterior wall. It will be noted that this is the reverse of the figures returned by a consideration of the total acidity above.

TABLE XV.—Relation of Free HCl to Location of Ulcer Found at Operation.

Location . . .	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total
Pyloric . . .	2	2	7	10	13	11	6	5	5	0	2	63
Prepyloric . . .	1	2	0	0	1	0	1	0	0	0	0	5
Lesser curvature . . .	3	1	9	7	12	7	2	1	0	0	0	42
Near cardia . . .	0	0	2	4	2	0	0	0	0	0	0	8
Posterior wall . . .	1	0	3	3	2	0	2	0	0	0	0	11
Anterior wall . . .	0	0	1	0	0	0	1	0	0	0	0	2
Totals . . .	7	5	22	24	30	18	12	6	5	0	2	131

SUMMARY.

Average free HCl—pyloric ulcers	46.5
Average free HCl—lesser curvature ulcers	38.8
Average free HCl—ulcers at or near cardia	35.0
Average free HCl—ulcers on posterior wall	36.8
Average free HCl—ulcers on anterior wall	45.0

Both tables demonstrate that location of ulcer plays a relatively small part as a local "irritative" factor in the production of acidity. The figures returned also show that while high total acidity and free HCl are occasionally met with in gastric ulcer of the class under consideration, they are the exception rather than the rule.

(f) *Combined Hydrochloric Acid.* Table XVI makes evident that in food retention-free gastric extracts combined hydrochloric acid can be almost constantly demonstrated. There is relatively little difference between the amounts where ulcers are variously located. Our series showed a slightly lower average where ulcers were at the cardia than when such were at the pylorus or on either wall of the stomach.

TABLE XVI.—Relation of Combined Acidity to Location of Ulcer Found at Operation.

Location . . .	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total
Pyloric . . .	12	45	5	1	63
Prepyloric . . .	1	3	1	0	5
Lesser curvature . . .	13	25	4	0	42
Near cardia . . .	0	7	1	0	8
Posterior wall . . .	3	3	5	0	11
Anterior wall . . .	1	0	1	0	2
Totals . . .	30	83	17	1	131

SUMMARY.

Average combined acidity in ulcer at pylorus	14.2
Average combined acidity in ulcer of lesser curvature	12.8
Average combined acidity in ulcer at or near cardia	12.5
Average combined acidity in ulcer on posterior wall	16.8
Average combined acidity in ulcer on anterior wall	15.0

(g) *Relation of Free HCl Content to Age of Patient.* Table XVII details the result returned by this study. It will be seen while the highest average acidity is shown in the group of ulcers occurring in the third decade, quite comparable averages are returned by analyses in patients in the sixth and the eighth decades. In no decade are the averages very low:

TABLE XVII.—Relation of Acidity to Age of Patient.

Age and number.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total with meals.
0-10 ⁰ . . .	0	0	0	0	0	0	0	0	0	0	0	0
10-20 ⁰ . . .	0	0	0	0	0	0	0	0	0	0	0	0
20-30 ²¹ . . .	1	0	1	4	6	4	3	0	0	0	2	21
30-40 ³⁸ . . .	2	2	8	7	6	4	4	1	2	0	0	36
40-50 ³¹ . . .	4	1	5	6	6	2	1	1	3	0	0	29
50-60 ³⁹ . . .	0	2	7	6	7	6	4	4	0	0	0	36
60-70 ³⁸ . . .	0	0	2	2	1	1	0	0	0	0	0	6
Over 70 ³ . . .	0	0	0	1	1	1	0	0	0	0	0	3
Totals . . .	7	5	23	26	27	18	12	6	5	0	2	131

SUMMARY.

Average free HCl—age 20 to 30	48.2
Average free HCl—age 30 to 40	41.1
Average free HCl—age 40 to 50	39.3
Average free HCl—age 50 to 60	45.0
Average free HCl—age 60 to 70	36.6
Average free HCl—age over 70	45.0
Average free HCl for all ages	42.5+

(h) *Relation of Free HCl Acidity to Pain Time.* The information returned by Table XVIII is suggestive. It is apparent that following food ingestion a progressively increasing number of cases show pain manifestations up to the fourth hour. Between the third and fourth hours, the greatest number complained of distress. The summary of average acidities shows that the degree of acidity increases up to the fourth hour after eating. It would seem that this series furnishes instructive data respecting relation between distress and concentration (?) of free HCl. After the fourth hour there is a progressive diminution in acidity, a correspondingly less number of cases manifest pain in these periods.

Where continuous distress is complained of the average acidity does not appear to be as high as where definite periods of pain following food ingestion are evidenced.

TABLE XVIII.—Relation of Free HCl Acidity to Pain Time.

Time and group.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total.
1. Immediately, P. C. . . .	1	0	0	1	1	1	0	0	0	0	0	4
2. Less than 1 hr., P. C. . . .	2	0	2	5	2	1	3	1	0	0	0	16
3. Less than 2 hr., P. C. . . .	1	1	2	5	5	3	2	0	0	0	0	19
4. 2 to 3 hrs., P.C.	0	0	9	7	3	4	5	2	2	0	0	32
5. 3 to 4 hrs., P.C.	0	2	3	2	12	5	1	1	2	0	2	30
6. 4 to 5 hrs., P.C.	0	0	3	2	2	2	0	1	1	0	0	11
7. Over 5 hrs., P. C.	0	0	2	0	1	0	0	1	0	0	0	4
8. Irregularly . .	2	1	2	3	1	0	1	0	0	0	0	10
9. Continuously .	1	1	0	1	0	2	0	0	0	0	0	5
Totals	7	5	23	26	27	18	12	6	5	0	2	131

SUMMARY.

Group 1—average free HCl	36.6
Group 2—average free HCl	40.3
Group 3—average free HCl	40.3
Group 4—average free HCl	46.0
Group 5—average free HCl	51.3
Group 6—average free HCl	46.0
Group 7—average free HCl	42.5
Group 8—average free HCl	29.0
Group 9—average free HCl	33.0

Relation of Free HCl to Vomiting: Table XIX shows that more than 60 per cent. of all cases that vomited had free HCl between 20 to 50. The average was 35.1.

Of the non-vomiting class, but 46 per cent. are grouped between acidity 20 to 50. Their average free HCl was 37+.

More than 56 per cent. of the cases giving no history of vomiting had free HCl between 40 to 80. The average in this group was 57.

(i) *Relation of Free HCl to Hemorrhage.* Table XX demonstrates that 57 per cent. of ulcers evidencing *hematemesis* had acidity between 20 to 50. The average acidity was 35+.

More than 57 per cent. of cases giving no history of hemorrhage had acidity between 30 to 60. The average acidity was 46.

Melena. Sixty per cent. of cases had acidity between 20 to 50. The average acidity was 36+.

TABLE XIX.—Relation of Acidity to Vomiting. Free HCl.

Group.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total.
Vomited . . .	3	4	20	20	20	12	10	3	5	0	2	99
No vomit . . .	3	1	3	6	6	6	2	4	1	0	0	32
Total . . .	6	5	23	26	26	18	12	7	6	0	2	131

TABLE XX.—Relation of Acidity to Hemorrhage. Free HCl.

Group.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total.
Hematemesis . .	2	1	6	14	6	5	5	3	2	0	2	46
No hemorrhage . .	5	2	13	11	17	14	6	2	3	0	0	73
Melena . . .	0	1	2	1	3	1	1	1	0	0	0	10
Totals . . .	7	4	21	26	26	20	12	6	5	0	2	129

(j) *Relation of Free HCl Acidity to Character of Ulcer.* Reference to Table XXI demonstrates that the highest acidities are associated with perforated ulcers. The highest average acidity is shown to be associated with subacute perforating ulcer.

TABLE XXI.—Relation of Free HCl Acidity to Character of Ulcer.

Group.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total.
Subacute perforating	0	0	1	0	1	2	2	1	1	0	1	9
Chronic perforating	1	1	1	3	2	4	0	0	0	0	0	12
Chronic perforating with adhesions	0	1	5	9	5	2	3	3	1	0	1	30
Indurated calloused	6	1	11	13	15	8	7	1	4	0	0	66
Saddle	0	1	3	1	2	2	2	1	0	0	0	12
Saddle with adhesions	0	0	1	1	0	0	0	0	0	0	0	2
Totals . . .	7	4	22	27	25	18	14	6	6	0	2	131

SUMMARY.

Subacute perforating, average acidity	64.1
Chronic perforating, average acidity	39.1
Chronic perforating with adhesions, average acidity	46.6
Indurated calloused, average acidity	42.1
Saddle, average acidity	43.3
Saddle with adhesions, average acidity	30.0

(k) *Relation of Free HCl Acidity to Nausea.* In 12 instances nausea was a distressing feature. Half of this number had free HCl between 20 to 50. The average acidity of this class was 36.6. The average acidity of the entire group was 49.5.

(l) *Relation of Free HCl Acidity to Pyrosis.* In 22 instances, pyrosis was a prominent symptom. More than 67 per cent. had acidity between 30 to 70. The average of this class was 47+.

TABLE XXII.—Relation of Free HCl Acidity to Nausea.

Group.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total.
Nausea . . .	1	1	2	1	3	0	1	1	1	0	1	12
No nausea . . .	6	4	21	25	24	18	11	5	4	0	1	128
Totals . . .	7	5	23	26	27	18	12	6	5	0	2	140

TABLE XXIII.—Relation of Free HCl Acidity to Pyrosis.

Group.	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100	Over 100	Total.
Pyrosis . . .	0	0	2	5	4	3	3	1	2	0	2	22
No pyrosis . . .	7	5	21	21	23	15	9	5	3	0	0	118
Totals . . .	7	5	23	26	27	18	12	6	5	0	2	140

5. OPERATIVE FINDINGS. (a) *Location.* Table V demonstrates the number of ulcers in each situation as found at laparotomy. It will be noted that the pylorus proper was involved in 65 instances (46.4 per cent.), while in 75 cases (53.6 per cent.), the ulcer was in other portions of the wall of the stomach. In 2 instances two ulcers each were found.

(b) *Character of Lesion.* The tabulations already made (Tables XI and XXI show in detail the number of each class of ulcer found on laparotomy. In addition to this general clinical classification, we may state that of the 50 ulcers which were available for microscopic examination, 12 (24 per cent.) were noted as active "inflammatory," 6 (12 per cent.) showed beginning carcinoma. The remaining 32 were indurated or "calloused" ulcers. In 5 cases an existing or suspected lues was an etiologic and prognostic factor.

(c) *Extragastric Lesions Demonstrated upon Laparotomy.* Appendix: In 49 instances (35 per cent.) sufficiently marked evidences of disease were found in the appendix as to warrant its removal. It has already been stated above that 8.5 per cent. of the cases in this series had had appendectomy before coming to the Clinic. The combined figures, 43.5 per cent., indicate that more than two-fifths of all patients of this group had appendix alterations. The observation is sufficiently striking to warrant emphasis from at least three points: (1) The etiologic relation between appendix alterations and coincident or subsequent changes in the stomach wall; (2) the prognostic limitations respecting normal gastrointestinal function following appendectomy; (3) the advisability

of careful anamnesis and upper abdominal examination of individuals whose only ailment, symptomatically, appears to be located in the right lower quadrant.

Gall-bladder: Operatively, cholecystitis and cholelithiasis were demonstrated in 21 (15 per cent.) individuals. Previous to entering the Clinic, 7.8 per cent. of the patients in this series had already had operations for gallstones or cholecystitis. The combined statistics indicate that 22.8 per cent. had alternations in the gall tract, apart from gastric pathology. Combining the figures from observations upon the appendix and gall-bladder it is seen that nearly two-thirds (66.2 per cent.) of the cases in this report had associated with definitely proved gastric disease, anomalies of these divisions of the digestive mechanism. In addition to the above, Lane kink was found twice, carcinoma of the gall tract once, and pancreatitis four times (2.8 per cent.).

(d) *Operative Procedures.* Table XXIV offers significant information respecting operative versatility required to meet the particular anomaly in the given subject in order to secure maximum results.

TABLE XXIV.

Operation.	Number of cases.
Posterior gastro-enterostomy (Mayo)	49
Gastro-enterostomy + excision	14
Gastro-enterostomy + sutures	24
Excision alone	24
Compression sutures	5
Anterior gastro-enterostomy	4
Pylorectomy or resection without or with gastro-enterostomy	4
Finney	3
Finney + sutures	1
Heinke-Mikulicz without or with gastro-enterostomy	4
Billroth No. 2 + posterior gastro-enterostomy without or with excision	3
Infolding of ulcer	3
Jejunostomy + Witzel	1
Unclassified (plastic)	1
Total	140

In view of Cannon's recent work upon gastric peristalsis, it would appear that choice of operative procedure to fit the case in hand is quite as essential as is the recommending of patients to submit to laparotomy. Table XXIV emphasizes this.

In this series 2 (1.4 per cent.) cases died within a month following operation. One case had chronic perforating ulcer, with adhesions, who developed obstruction, following extensive excision. The other case was one of large perforating posterior wall ulcer, with adhesions involving the pancreas.

The records show that another patient died five months following excision of a perforating anterior wall ulcer, while two years following excision of a posterior wall ulcer a fourth patient succumbed

to general sarcomatosis, primary in the pancreas. To July 1, 1912, no other deaths had been reported.

(e) *Secondary Operations.* Six cases required second operation within one and a half years following the primary laparotomy. The conditions were as summarized in Table XXV. With the exception of the case later developing a duodenal ulcer, the ulcers requiring the second operation were rather unusual either as to character or situation.

TABLE XXV.

Primary operative finding.	Primary operative procedure.	Second operative procedure.
Ulcer of posterior wall and hour-glass stomach	Billroth No. 1 and excision	Posterior gastro-enterostomy for obstruction.
Large calloused ulcer at pylorus . .	Infolded	Posterior gastro-enterostomy.
Ulcer at pylorus with marked adhesions	Finney	Posterior gastro-enterostomy.
Ulcer at pylorus, with subacute perforation to head of pancreas . .	Excision	Posterior gastro-enterostomy.
Ulcer at base of anterior wall . .	Posterior gastro-enterostomy	Duodenal ulcer. Excision, plastic.
High perforating ulcer on lesser curvature	Excision	Posterior gastro-enterostomy.

SUMMARY. The above clinical analysis of 140 cases of operatively demonstrated surgical gastric ulcer without food retention appears to warrant the following statements:

1. In more than one-third of operatively demonstrated gastric ulcers the stomach's emptying power is maintained.

2. 92 per cent. of this group of ulcers occurs between the ages of thirty and sixty. Males are affected three times as frequently as females. The American-born farmer furnishes a large number of gastric ulcers.

3. Irregularity of food ingestion with the use of alcoholic stimulants is not an uncommon concomitant of gastric ulcer.

4. A rather striking frequency of history of previous infectious disease is shown. 18.9 per cent. of our cases had had typhoid fever.

5. A mild grade of secondary anemia is present in the average gastric ulcer.

6. Weight loss averaging more than twenty pounds without marked cachexia was shown in this series. The loss may be so rapid as to frequently suggest malignant disease. Some cases consistently gain weight.

7. Appetite is lost or is capricious in nearly three-fourths of the cases. More than 65 per cent. are constipated.

8. Nearly three-fourths of the cases have "spells" or "attacks" of discomfort, with good health between such. Such a history may extend over thirty years without alarming clinical manifestations. The attacks are usually called "biliousness" or "dyspepsia." They often show a peculiar seasonal relation. In 36 per cent. of

instances the disability is continuous, with or without nutritional disturbances.

9. Abdominal pain or distress is a constant symptom in gastric ulcer. It is "colicky" in nature in more than 22 per cent. of cases, requiring hypodermic medication in 12.7 per cent. It is frequently mistaken for appendix, or gall-bladder disease, and is often associated with such in addition to gastric ulcer. Night pain, with interference with sleep, is present in 19.2 per cent. of cases. 80 per cent. of patients complain of epigastric distress, frequently referred to the right rib margin or the back.

In 87.8 per cent. of proved ulcers, pain, or distress has definite relation to food ingestion. 83 per cent. of cases show pain or distress coming on within four hours following eating. Nearly two-thirds of pyloric ulcer cases have discomfort from two to four hours after eating, more than one-half of lesser curvature ulcers from one to three hours after eating, more than two-thirds of posterior wall ulcers within three hours after eating, and more than two-thirds of ulcers near the cardia less than two hours after eating, while more than 44 per cent. of this class less than one hour after eating.

Discomfort is most frequently controlled by ingestion of food, alkalis, and by vomiting. 12.2 per cent. required morphine.

On palpation, epigastric tenderness is exhibited in 95 per cent. of cases. In more than three-fourths of our series, tenderness was most marked in the right upper abdominal quadrant. 2.8 per cent. of cases showed palpable ridges.

More than four-fifths of the ulcers were located at the pyloric half of the stomach, and this was in general the anatomic area of greatest complaint or distress on examination.

The diagnosis of the character of ulcer to be found on exploration is only possible where a careful anamnesis is made.

10. Vomiting is present in nearly three-fourths of gastric ulcers without food retention. About 17 per cent. vomit food. Only rarely is delayed vomiting observed. Vomiting is induced in more than 10 per cent. of cases to relieve pain. Nearly 40 per cent. of patients vomit regularly. "Waterbrash" is a prominent feature in 19 per cent.; pyrosis and eructation in 87.8 per cent. In nearly one-third of the cases, vomiting comes at the time of maximum abdominal distress. In 28 per cent. the ingestion of food precipitates vomiting; more than 53 per cent. vomit within three hours after eating. In 7 per cent. night vomiting is a feature. Ulcers at the pyloric half of the stomach are most commonly associated with vomiting even when there is no interference with the emptying power of the stomach.

11. *Hemorrhage*. Of 140 proved ulcers in this group, bleeding (hematemesis or melena) was noted in but 40.7 per cent. About

one-fourth of the cases had hematemesis alone, one-third hematemesis with or without melena, while 7.1 per cent. had melena alone.

Severe hemorrhage or frequently repeated moderate hemorrhages are usually associated with faint feelings or actual fainting (40 per cent.).

Hematemesis is more frequent than melena, but melena alone may occur entirely independent of the location of the ulcer. While bleeding is associated with any type of ulcer, nearly two-thirds of those doing so show operative evidences of perforation.

12. *Test-meal Findings.* Acidity: Irrespective of location of the ulcers the average total acidity was 55; the average free HCl, 42.5; the "combined" HCl in 82 per cent. of cases between 10 and 20. Total acidity is most commonly higher in ulcers involving the lesser curvature and anterior wall than where other parts of the stomach are affected. High free HCl is noticeably more frequent where the ulcer is at the pylorus. While high free HCl is usual in cases in the third decade of life, this is not the rule.

Following food ingestion the great majority of cases show pain within four hours. This series shows that during this period free HCl is progressively increasing. Patients complaining of continuous distress do not necessarily have high acidity.

Vomiting is not usually associated with high free HCl. More than half of the non-vomiting cases had higher acidity than was the average of those vomiting. The average free HCl of patients bleeding was 35+. More than half of the cases giving no history of hemorrhage had average free HCl of 46.

The highest free HCl averages are associated with subacute perforating ulcer.

13. *Operative Findings.* More than two-fifths of the ulcers were at the pylorus.

Of 50 ulcers microscopically examined in this series 24 per cent. showed active inflammatory change, 12 per cent. early carcinoma.

In 35 per cent. of cases, diseased appendix was associated with gastric ulcer. In 15 per cent. cholecystitis and cholelithiasis were demonstrated as concomitant processes. In nearly two-thirds of this group of gastric ulcers, diseased appendix and gall-bladder were revealed operatively. In view of these figures it is evident that all laparotomies should be thoroughly exploratory even when a well-marked gastric ulcer has been demonstrated.

Operative procedure should be adapted to the individual finding on exploration. A routine technique is frequently accountable for poor post-operative progress.

Prompt relief of symptoms with a comfortable after course is the rule following operative treatment of retention-free ulcer cases.

This series shows an operative mortality of 1.4 per cent. Rather more than 4 per cent. required a second operation. This usually occurred in uncommon cases.

THE ECONOMIC ASPECTS OF HOOKWORM DISEASE IN PORTO RICO.¹

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THE island of Porto Rico, with its 3606 square miles of territory and 1,120,000 inhabitants, is almost exclusively devoted to the culture of sugar, tobacco, coffee, and fruit, named in the order of their importance in 1912; sugar in the coast lands, tobacco in the foothills and some mountain valleys, and coffee in the mountainous regions. As fully three-quarters of all labor performed on the island is agricultural, and the output of each plantation depends largely upon the laboring capacity of those engaged in tilling the soil, given the fact that all vegetation is luxuriant and no serious natural conditions hinder the raising of large crops, a study of the great scourge of the laboring classes, uncinariasis, will throw a flood of light upon heretofore obscure factors in the economic development of Porto Rico during the last fifteen years, perhaps through centuries preceding this period.

The value of the coffee crop in 1897, American gold, was \$7,492,453; that of sugar, \$2,456,898; and that of tobacco, \$732,117. Coffee formed 70 per cent. of the value of all the exports in 1895 to 1897 and 41 per cent. of all cultivated land was devoted to its production.

In 1910 the value of sugar exported was \$23,545,922 (representing over 60 per cent. of all products leaving the island); coffee, \$5,669,602; and tobacco, \$5,664,128.

The total value of articles purchased from and exported to the United States in 1901 was \$17,502,103, and in the fiscal year 1910, \$68,595,326, a gain within ten years of 400 per cent.

Thus we see sugar today the life-giving product of Porto Rico with an increase of seventeen-fold its value in 1897; tobacco a promising industry, which is seven and one-half times as important as formerly, and coffee a decadent industry, which has but 75 per cent. of the value it possessed in the days of Spain.

Our study cannot embrace a detailed consideration of the economic problem, but let it suffice to say:

1. That sugar rose in value when it came under the protective tariff of the United States. Coffee fell when Spain's preferential tariff was removed, and, although the bean was of a superior class, it was unknown and unappreciated in the only free market open to it, the United States, where it had to compete with cheap grades.

¹ Read before the Fifteenth International Congress of Hygiene and Demography, Section 4, Industrial Diseases, held in Washington, September 23 to 28, 1912.

2. That the output of sugar was enormously increased by improved methods of culture and by great mills, now among the largest of their kind in the world. Coffee culture has progressed very little, if any, in improved methods: (1) because, from the nature of the industry, machinery plays an unimportant part in its preparation for the market; (2) because the coffee planters were so poor they were unable to keep their estates at anywhere near their full productive capacity, the bushes needing constant manual attention to increase their output. The value of the crop often barely sufficed to pay the interest on their mortgages, and was totally insufficient to meet the expense of improvements tending to increase their production, especially as loans could only with great difficulty be floated.

3. Sugar rose to the surface in an increasing era of prosperity, unhampered by any convulsion of nature, and favored by the benign influences above cited. Coffee planters were surprised by the war in the midst of speculation and borrowing. Their estates, and even their ripening crop, heavily mortgaged, were visited one year after the American occupation by a disastrous hurricane, which dashed to the ground in a day the coffee bushes, and, worst of all, the shade trees, which are necessary for the superior quality of the bean, thus precluding resuscitation of former crop values for at least five years. Many other factors which tended to depreciate the industry might be mentioned, but a fourth element of highest importance remains to be noted:

4. Sugar lands, and, to a less extent those of tobacco, bereft of shade and bathed by a hot sun, are notoriously poorer culture grounds for *Necator Americanus* than those of coffee. They are far drier, are well ploughed, and well drained. Coffee groves, well shaded, always sopping and generally undrained, and, above all, far more densely worked, are among the most perfect culture grounds for this parasite in the world. Moreover, the laborers in sugar estates were chiefly negroes, who are relatively immune to uncinariasis. They were and still are better paid, better housed, and better clothed than the poor white coffee laborer, with a constitution weakened by chilling, damp winds, insufficient clothing, insufficient and improper food, and general poverty and wretchedness.

The result has been that the lands previously cultivated in tobacco and coffee have been encroached upon by sugar wherever possible, and that tobacco, increasing in importance, has seized upon coffee lands which are materially diminished in area and driven clear to the mountain fastnesses, where they are generally isolated by lack of roads over which to bring their products to the coast.

We are now in a position to understand why the coffee crop in 1901 was valued at but \$1,678,765. In 1904, in part due to partial

recuperation of the coffee groves after the hurricane and in part to better prices, it was valued at \$3,903,257. From 1904 on the area of land under cultivation for coffee has steadily diminished, and yet the crop has as steadily increased, until in 1910 it was valued at \$5,669,902. This means practically but one thing—increase in production. It has not been great, but it is perceptible.

Those who are conversant with affairs in Porto Rico will realize the precarious condition of her commercial future when one reflects that upon one product—sugar, and the market price of that product—depends her prosperity. Sugar is today, relatively speaking, where coffee was in 1897. Let the duty fall from sugar, and tobacco, as yet a weak industry, and coffee, a struggling one, must together support the island. Sugar this day is the mainstay of Porto Rico, but it is far from being the workingman's ideal crop. Only rich men and powerful corporations can grind sugar. Only the large ones financially can supply these mills with sufficient cane to make them pay. Coffee is the country gentleman's crop, the poor man's crop, the Porto Rican's crop. Even when coffee brought but \$7,500,000 a year to Porto Rico, the "jibaro," or poor white coffee laborer, was "better off." His dollar "went farther." Coffee holdings are small holdings, and they well distribute wealth here. Why was coffee so depressed when every other industry was booming? No one can justly complain of prices which permit good profit, and at present the price of coffee is nearly what it was in 1895-1897, when the industry was flourishing. The answer of coffee planters is concise: "There was no coffee!" What they mean is that the per acre production was utterly inadequate. That this is improving is seen in figures above cited. The improvement is attributed by some to this factor, by others to that, but no one, no matter how prejudiced, fails to realize that healthy, strong, and abundant labor plays a tremendous part in the future of the coffee industry in the island of Porto Rico.

Thus we can establish the inseparable relation of the health of the coffee laborer to the welfare of the industry; thus we, as medical men, can justly lay claim to a share in the awakening of that industry which in its palmy days brought happiness and contentment to the people of Porto Rico, for in 1904 a campaign was instituted against "anemia," or uncinariasis, the chief cause of the invaliding of the Porto Rican laborer, especially of the coffee laborer, which has culminated in the successful treatment of 300,000 persons of this class. No Porto Rican is capable of denying to the forty or fifty physicians whose efforts through six years have accomplished this result a part in the financial betterment of their people after this tremendous campaign.

Dividing the island into the municipalities bordering on the coast and those of the interior we find that of the former, out of a total population of 618,871 persons, 117,989, or 19 per cent.,

were treated for uncinariasis; and that of the interior, 130,989 of a population of 334,372, or 39 per cent., were so treated. A little over 50,000 were migratory, and their residence could not be fixed. The unit of division, politically speaking, is the municipality as is the county in the United States; but topographically, while the twenty-four interior municipalities are in the highlands, chiefly devoted to coffee culture and secondarily to tobacco, a considerable part of the area of a coast municipality is apt to extend well back into the mountains, and, of course, such territory is given over to coffee. So it may be said, without fear of error, that not over one-tenth of those seeking treatment for their anemia were sugar laborers, not over one-fifth tobacco workers, and the rest came from coffee groves.

In the rehabilitation of this coffee industry only one plan is feasible: to increase the per acre production, and to do this workmen capable of 100 per cent. of labor daily are needed. Until anemia among this class is thoroughly under control this will be impossible.

THE LABORER. He is a tiller of the soil, pure and simple, living by sufferance in a rude hut he built, but whose ground he does not own. With a large family he is powerless to save any of his earnings, and, as Weyl puts it, it would be a crime for him to attempt it. When not a victim of anemia he is usually a well-nourished, well-built man of medium stature, reserved, suspicious of strangers, unschooled but astute, generous, and respectful. Again eliminating anemia, his diseases are few, as are his vices. He is long-suffering, and, above all, hardworking, but his methods of labor are primitive and wasteful. He is totally dependent upon the outcome of the crop he labors to realize, and, not being a landowner, unable to read and write, he looks to the planter he serves for protection and ideas.

In the mountains he is a coffee laborer and a white man. On the coast he is more frequently a negro or a mulatto, notwithstanding the tendency of late years for the white coffee laborer to work in the sugar fields during the inactive season in the coffee plantation. His food is confined practically to native vegetables and fruits, with rice, codfish, coffee, and condiments. His diet lacks animal proteids and fats, and would be considered below par in Europe and North America. Take away his wages and he lives from hand to mouth on native fruits and vegetables, for rice, codfish, and condiments he must buy.

That Spain's protection of coffee merely brought about a value of \$7,500,000 in 1897, when in 1911 \$5,500,000 was rendered by far less coffee land, without any protection and with the stormy past already recounted, must be considered notable. Something was certainly missing. When we consider that from 1890 to 1899 the percentage of deaths from "anemia" to the total death rate

gradually climbed from 13 to $22\frac{1}{2}$ per cent.; when we take into account the testimony of druggists and physicians practising in those days to the effect that they flourished, due to the generous sums spent to secure medicine and medical attendance by the laborer; when we realize that when 15 per cent. of the total death rate is due to anemia, the hemoglobin of the average laborer is not far from 50 or 60 per cent.; we cannot but see that Spain's best endeavor fell short from her failure to solicit medical coöperation. Could sugar have attained a value of \$25,000,000 a year with a laborer whose hemoglobin is but 60 per cent.? We believe not. A sugar planter fights shy of a physical wreck when he is looking for his laborers, for the work is hard and requires strong men.

When we Americans first landed in Porto Rico our attention was attracted by the muddy yellow pallor of the average laborer in the country. The anemia of uncinariasis is really a rare cause of death in Europe and North America. Even severe cases are, apparently, very uncommon. What is justly feared is the diminution in laboring capacity. But in Porto Rico, with about 300 persons to the square mile, with ideal cultural conditions for the larvæ, and with small coffee estates in whose shady groves hundreds of barefooted workers daily congregate, clearing underbrush or picking coffee and continually befouling the soil, each laborer receives an almost daily dose of *Necator Americanus*, a series of multiple infections that fairly break through the most impervious natural immunity and leave an entire class anemic, with a frightful death rate, impossible to comprehend outside of Porto Rico. When it can be said that 30 per cent. of all deaths occurred from anemia in 1900, and that over 60 per cent. of these deaths occurred in the mountains, that two of every hundred died yearly of uncinariasis, has anyone any doubt about the physical condition of the other ninety-eight who lived and were infected under the same conditions as the two unfortunates who lost their lives?

To be more explicit: The hemoglobin of 577 persons presenting themselves for treatment in the Bayamon dispensary in 1904 averaged 43.09 per cent. This was at the beginning of our campaign, and is an especially valuable note, because Bayamon is a coast town where anemia should have been least prominent, but which nevertheless represented the laboring class of sugar, tobacco, and fruit estates, the industries of that rich municipality at that time.

In the same campaign of 1904-1905, of a total of 5490 treated personally by myself and two associates, 22 per cent. were light or very light cases; 19 per cent. were moderate; 41 per cent. were intense or very intense, and 18 per cent. were unclassified. In the six years' campaign, in which 287,528 persons were treated,

3.99 per cent. were very light cases, 20.39 per cent. light, 44.90 per cent. medium, 25.05 per cent. intense, and 4.68 per cent. very intense. There was 0.96 per cent. unclassified. When we consider that we did not classify these cases by hemoglobin percentage in the majority of instances, there may be some objection raised to any attempt at classification; but when we also note that our dispensary physicians had become familiar with the clinical types throughout their life in Porto Rico, and were keen at placing the cases in the class they belonged, it will be seen that the error, if there was any, was exceedingly slight. This we know from our own experience, where a series of several thousands were subjected to a hemoglobin examination at the beginning of the work. Our classification by hemoglobin percentage was as follows:

Between 60 per cent. and normal, a light or very light case.

Between 30 and 60 per cent., a medium or moderate case.

Below 30 per cent., an intense or a very intense case.

The clinical estimate of the grade of the disease was as follows:

A light case: An individual, previously vigorous and energetic, gradually finds himself losing in strength and inclination to work, with symptoms of dyspepsia and perhaps a faint pallor. To his friends and neighbors he is "run down." To unfriendly eyes he is "lazy and good-for-nothing."

A moderate case: A moderately anemic individual, with minus activity of mind and body. The patient looks and feels definitely sick. There is no longer mere disinclination to work, but partial inability. He is pale, exertion brings on throbbing of arteries and palpitation of the heart; sudden changes of position, sudden dizziness. He is half narcotized, as it were.

An intense case: The patient has arrived at that stage when a fatal termination may occur at any time. Extreme pallor, edematous extremities, dilated heart, etc.

On referring to the 5490 cases of 1904, where the taking of hemoglobin percentages on admission was often practised (upon which percentage the type of the disease was based), and comparing this result with the estimate of the case as established clinically in over 280,000 cases subsequently treated, it will be seen that by the latter method the seriousness of each case was rather apt to be underestimated than overestimated.

In whatever light we choose to view it, we can see how sick a laboring class Porto Rico had. My own experience has led me to consider the hemoglobin percentage a fair estimate of laboring capacity between 20 and 85 per cent., although it is wonderful to see the work attempted by an anemic laborer. Below 20 per cent. he is usually *hors-de-combat*, and above 85 per cent. speculation concerning his laboring capacity as affected by the worm he harbors is too uncertain. This means that the average anemic working-

man in Porto Rico lost at least 50 per cent. in working capacity from "anemia."

This unrecognized disease from earliest colonial days has been responsible for the unjust charge of the full-blooded European that the Porto Rican laborer was lazy and indolent, and only after a tremendous cyclone, which threw the coffee-worker upon his own resources, was the mask snatched from the face of one of the most pitiful situations known to medical history. When urged by the planter, by the insular government, by the American people, to arise and go to work, he laid down to die in large numbers, at last incapable of responding to even dire necessity.

Anemia in Porto Rico, influenced by the special conditions incident to the downfall of coffee and by the thousand and one factors which go to weaken the resistance of a defenceless and poverty stricken people to a chronic exhausting disease, deeply affects the laborer, the landowner, and the territory.

The Effect of Uncinariasis upon the Laborer. 1. To reduce his earning capacity: Many times he is paid for the work he accomplishes in a day. This is eminently true of coffee-picking, where he receives from ten to fifteen cents per almud or conventional box-full. Some planters have two sets of wages: one for a healthy man and another much lower, for an anemic. Incidentally they state that they lose money on the anemic, even with his lower wage, but have not the heart to discharge him and so retain him in the hope that he may be cured and swell the numbers of his no-too-numerous workers.

2. To sap his scanty wage from the purchase of medicines and, in some cases, from doctor's fees: The amount of patent blood restorers sold in Porto Rico in past years is astonishing. When finances here were at their lowest ebb after the cyclone this ghoulis industry saw its best days. Doctors could not possibly reach the sick rural population, even had they desired, for the municipal doctor has on an average 15,000 people to attend, often more. These were practically all indigent, and 70 per cent. were more or less sick. They lived not in town or hamlets, but in every nook and cranny of the municipality, nine-tenths of whose population was distributed throughout the rural districts, unapproachable by roads, and generally reached alone over breakneck trails. Over five visits a day to such sick was impossible, and only the few fortunate ones had a modest fee to tempt a physician's call. The rest had to depend upon the lying promises of patent medicines and charlatans.

3. To clog his mentality and reduce his spirit: "Over all the varied symptoms with which the unfortunate jibaro, infected by uncinaria, is plagued, hangs the pall of a drowsy intellect, of a mind that has received a stunning blow. . . . There is a hypochondriac, melancholy, hopeless expression, which in severe

cases deepens to apparent dense stupidity, with indifference to surroundings and lack of all ambition."²

Such people are unable to act on their own initiative, and have to be driven to work and told each thing separately several times before they understand.

4. To prevent him from avoiding infection: The earnings of a family averaged in 1904 according to Weyl, the expert of the Department of Commerce and Labor of the United States, considerably less than \$100 a year, and there was work available upon only four days in the week. Nine months in the year the majority had no steady work and during the other three months, or at the time of the coffee harvest, the whole family was employed and payment was made, in coffee plantations at least, according to amounts picked. Fifty per cent. of a normal picking was 50 per cent. lost directly from disease. Should every cent of his earnings be spent for food, his ration would still be inadequate for his working necessities. In this way shoes were an impossible luxury. His miserable physical and mental condition, lack of market from impassable roads, lack of beasts of burden with which to work, made cultivation of garden patches out of the question.

5. To prevent his seeking employment elsewhere than in the coffee grove: Coffee laborers, sick with anemia, are not wanted on sugar plantations where there is less chance of infection and better pay. Thus his infirmity peonizes him and binds him to the grove.

The Effect of Uncinariasis upon the Planter. 1. If the roaming coffee picker could earn but a scant 50 per cent. of what he should earn in health, the regularly employed, living under practically the same conditions, could not be expected to earn more. As a matter of fact, even with the ridiculous wage paid in 1904 (thirty cents), the planter lost money in inefficient labor. In a visit made by me to a coffee plantation about two years ago, so remote from the stations for the treatment of anemia that the laborers were nearly all uncured anemics, I was told by the planter that he was thoroughly discouraged and was about to give up; that he had 1800 acres of the best coffee land, much of which he could not afford to put under cultivation, owing to the miserably insufficient output of the part already cultivated, and that he calculated his loss from sick laborers at about 50 per cent. It was then afternoon and the harvest time; the pickers were returning from the grove and depositing their day's collection in the mill. I stationed myself at the door and asked each one what his picking had amounted to on that day, having first established the normal amount which they should have picked per man. The average of some two hundred laborers was 50 per cent. short, and more, of what it should

² Uncinariasis in Porto Rico, Senate Document, No. 808, 1911, Government Printing Office, Washington, D. C.

have been, or two almudes a day. The amount received for a box full, or almud, varies with the abundance of berries, but on that day was twelve and a half cents an almud.

So here were two hundred people who had lost at least \$50 from a curable and preventable disease in one day. To have seen those poor rain-bedribbled, muddy, barefooted anemics one wondered how they ever brought in the coffee they picked, and, as a matter of fact, some stated that they had to be helped in by stronger comrades! Of these pickers many were pointed out to me as regularly employed peons of the estate, and these were indistinguishable from the rest, as far as the degree of their anemia went. When the incentive to make as large a picking as possible was only able to produce 50 per cent. of a healthy man's output, can we expect that these peons, working by the day and in the same physical conditions, should yield more for a wage?

2. With all the peons the planter could afford to pay, a large part of his estate remained uncultivated, or, if all cultivated, it would be so poorly worked as to yield only a fraction of its normal output.

3. The ideal of the planter is to secure enough peons to almost handle the crop, leaving a minimum to be employed at harvest time, for such itinerant laborers have to be provided for during two or three months in lodging, often for a meal, etc. The larger the number hired at harvest time the greater the expense aside from the wage. In the presence of an anemic peon class, no planter can make economic calculations on his crop.

4. There is at present a scarcity of labor in the coffee plantations. Many good laborers have left the plantation to seek employment in the sugar and tobacco fields, where the pay is better. But the men who leave are the cured cases of anemia, who otherwise would not be acceptable to the sugar estates. The result is that the planter in the mountains has to pay a higher wage than before, and still struggle with his anemics. This is a class that is rapidly disappearing, but the fact remains that it looks as though the coffee men would have to fight anemia to the bitter end, and long after the scourge will have ceased to become a serious menace to the success of the sugar and tobacco industries.

The Effect of Uncinariasis upon Insular and Municipal Government. 1. In a country where so large a percentage of the inhabitants live from hand to mouth, without any money saved for emergencies, in the presence of a disease which palpably affected 70 per cent. of the rural laborers, and caused in 1900 twelve thousand deaths, the resources of that country are strained to provide for them. About one-half of the insular taxes are covered into the insular treasury for roads, education, etc. Local roads, street construction, and other purely municipal expenditures have to be provided by the municipality. Were this municipality to provide for the proper

treatment of all its indigent sick, including expenditures for medicines, it would irremediably go bankrupt. As a matter of fact the paltry sums appropriated for this purpose never meet the situation. In many municipalities the proposals to furnish medicines for indigents were bid upon by local pharmacists, and in a month or so the entire amount was spent for the fiscal year. Even these sums of money, not always wisely spent and not large, represented, nevertheless, a great effort on the part of the poor town.

2. The property values naturally depend indirectly on the output, and when the properties are only partially developed the assessments fail to yield what they should.

3. The laborers employed by the insular government were apt to be the more anemic ones, the best having been absorbed by the plantations. In fact, these very sick were employed on roads at enormous expense at the time when it was supposed that their condition resulted from starvation, and as a measure of relief to the poor. No one can ever know what percentage of these appropriations was lost from inefficient labor.

When all is said and done, it is plain that to permit the coffee industry to die out in Porto Rico is really unnecessary, and very harmful. It is to many minds the crop of crops for the interior of Porto Rico, and its loss will ultimately spell ruin to sugar and tobacco, for these Antillan Islands, bared of their trees, become subject to long droughts and torrential washouts. This has actually happened, apparently, on the south coast, where a \$3,000,000 to \$6,000,000 irrigation plant is seeking to save Guayama, Salinas, and Ponce sugar. The mountains to the north are scarred and bare, and, for lack of the roots of bushes and the shade of trees to store up and gradually deliver by hundreds of little streams an ample water supply to the rich coast lands below, one of the richest sugar districts on the island is threatened. All of this aside from other considerations already mentioned.

Uncinariasis affects the whole island, directly and indirectly, but it is the chief bane of the coffee industry. To solve the coffee problem no plan is complete, nor would such a plan be successful, which takes no account of this medicosocial problem. In Weyl's report of labor conditions in Porto Rico in 1904 to the Department of Commerce and Labor of the United States we find the following:

"One of the most important of all the factors influencing the condition of the laboring classes of the island is the disease of anemia. This disease, which mainly attacks the poor of the island, more, perhaps, than any single factor, impairs the industrial efficiency of the great mass of Porto Rican laborers. The economic importance of the disease cannot be overestimated . . . the disease is so widespread as to be considered practically universal. The effect upon the conditions of the laboring classes of Porto Rico of completely obliterating the disease of anemia would be

almost incalculable. Many persons who are now too sick and weak to work would then be enabled to do so, and the industrial efficiency, as it is affected by the muscular strength, the nervous energy, the physical endurance, and the intelligent direction of work of the people would be vastly increased. An energetic movement with a view to the obliteration of the disease is probably the greatest single step which can be taken at the present time toward improving the industrial efficiency of the laboring classes of Porto Rico."

From 1904 to 1910 inclusive there have been treated for their anemia by a special service 300,000 persons in round numbers. This number will be much increased by adding the fruit of unofficial work, as follows:

1. Cases treated by physicians not connected with the service: Today there is hardly a physician who does not treat the anemic jibaro with thymol. Many times this is done without a previous fecal examination, in spite of our protests, but inasmuch as 99 per cent. of such cases are due to uncinariasis, great good results therefrom.

2. Cases treated by religious societies and medical missions: Their number is large, and they contribute in a most practical way to the general work.

3. Cases treated by charlatans: Remembering what has been said concerning the difficulty attached to reaching a doctor from the remote barrios of a municipality, is it any wonder that the more calculating jibaros learn the simple technique of treatment and apply it extensively for a consideration? That this is by no means uncommon is seen by skilful questioning throughout these barrios. A vigorous war upon these interlopers has been carried on from the first, but it is hopeless to expect to catch them all.

4. Cases treated by the family: The administration of thymol and salts for anemia is rapidly becoming a family remedy in certain parts, as quinine and calomel is in our South. Even some proprietors of estates are gingerly taking it up. Of course, this too is all wrong, but what can be more natural? Theoretically it is hard to obtain drugs without a physician's order, but in practice it is by no means difficult.

5. Cases treated by the officials of the anemia service in the intervals between appropriations to continue the work: On several occasions there was a hiatus between the ending of the fiscal year and the reestablishment of the anemia service. On one occasion the legislature was convoked in special session for the purpose of providing for the irrigation of the south coast and to reappropriate funds to continue the anemia work which it had failed to do at the regular session. In these intervals our physicians kept their stations open and worked without pay, although their records were no longer kept as they had been before. In addition to all

this there have been many thousand cases treated by the present sanitary service, which took over the work on July 1, 1910.

Hookworm disease probably gained its foothold in Porto Rico in 1530, nearly four hundred years ago. In 1788 Fray Iñigo Abbad states that "the jibaros had the color and aspect of convalescents." How many years this color and aspect had been observable he does not say, but we can safely affirm that for two hundred years Porto Rican anemia had been explained by the compound theory of improper food, tropical climate, and malaria.

To change the fixed belief of a people, the heritage of two hundred years, was no easy matter. From 1899, when this anemia was first identified by the writer as ankylostomiasis until 1904, when the real campaign against it began, was a period of hard work in propaganda and scientific study.

The result of the universal application of a specific remedy for this anemia has surpassed our most extravagant hopes. Today a bad case of uncinariasis is rare indeed along the highways of Porto Rico, where before in every town the traveler halted he was besieged by pitiful beggars in the last stages of the disease, unable to work and driven by hunger to implore charity from passersby. Few cases of moderate severity are seen, and, indeed, the color and aspect of the Porto Rican people can no longer be described as that of convalescents.

The mortality from anemia is but one-eighth of what it used to be. The total death rate has fallen from 42 per 1000 in 1899-1900 to about 22 per 1000 in 1912, and only in the mountains, in those far-away barrios unseen by traveler and even by the city-bred Porto Rican, does hookworm still stalk abroad, not indeed as it did before, for with the universal treatment of the disease came the universal education of the people, and today there is scarcely a jibaro who does not know that no one need die of his old enemy, "la anemia."

At the close of each year of work the Commission has made it a feature of the annual report to publish letters which demonstrate the enthusiasm and earnestness of those who worked with us to secure our ends. Until 1907-1908 our data had been secured from our physicians, who were really best fitted to judge of the results we were obtaining; but in the last-named year the municipal officials of thirty-seven towns, in each of which stations had been working throughout the year were called upon to express their opinion of the necessity for continuing the work. The Mayor, voicing the sentiments of the council, and, in some instances, the town council by formal resolution, eloquently appealed for its continuance, citing the improvement in the health of the people, the reduction in mortality, and the saving on the municipal budget for medicines. Many stated that they would gladly bear part of the expense to keep up the work, nine passed resolutions calling

upon the Governor to convoke the legislature in special session to appropriate funds enough to proceed with the campaign, and practically all paid a tribute to the work that amply repaid its physicians for the thousands to whom they had administered.

Thus we have the expressed approbation and support of the physician and of the people through their municipal officials. We have a demonstration, eloquent and persistent, of the jibaro's faith in this new "theory," which brought him daily in throngs over many a weary trail without the slightest compunction to our stations. We have the frank expression of the legislature, which from year to year has liberally supplied the necessary funds for the maintenance of the work to a total of nearly \$200,000. We have the earnest interest of all the governors of Porto Rico, beginning with Governor Hunt, in 1904, who together with the Honorable Regis H. Post introduced the first appropriation, to the present executive, Governor George R. Colton, all of whom have year after year urged upon the legislature the absolute necessity for supporting this campaign.

In short, no class nor condition of people in Porto Rico, hardly an individual, doubts the necessity of fighting anemia and of paying large sums of money to do so.

Notwithstanding all this, when I decided to write upon this subject it seemed to me that all of this testimony should receive that of the planter himself, who could perhaps say with even more certainty what these benefits have really amounted to. Accordingly, I addressed a circular letter to about 400 sugar, coffee, tobacco, and fruit growers representing every municipality in the island. Although the time is too limited since they were sent for me to have received answers from all, I give after each of the following questions the composite answer made by the 224 from whom replies have been received:

First question: "What percentage of laborers, who could perform a full day's work did you have on your estate in 1900?"

Answer: 40 per cent.

Second question: "What percentage of efficiency for labor have your peons gained since they have been cured of their anemia?"

Answer: 61.7 per cent.

Third question: "What percentage of anemic peons exist today on your plantation?" Answer: 17.5 per cent.

Fourth question: "Do you believe that by curing them your own profits would increase, and if so, by what per cent.?" Answer: Yes, by 40 per cent.

More than half spontaneously appended a warm and sincere expression for the results of the campaign; many demanding that it be kept up, and stating that the island legislature in all its history had never voted money that had been better spent.

I believe that the sentiment of the planter is best expressed by

the following letter (in answer to one of my own, enclosing a copy of the paper I am now presenting) from the president of the Coffee Growers' Association of Porto Rico:

"PONCE, P. R., July 15, 1912.

"DR. BAILEY K. ASHFORD, San Juan.

"My dear Sir:

"In answer to your circular of last June and your communication of the 12th instant, I desire to make the following observations:

"I have carefully read your interesting work on the economic aspects of the campaign against the anemia of this island, and I do not find anything to add to it, nor do I believe that I should have to make any correction in it. You have said everything. The results of this campaign should not be viewed solely in the light of the notable reduction in mortality shown by the statistics, so far as they refer to uncinariasis, but in the return to the sociologic normal of the large masses which the disease had rendered useless for work, in the work these masses are now contributing to our overincreasing production, in the number of human beings saved from beggary and the life of parasites, in the corresponding increase in our commerce, and in the general betterment of an important percentage of our people.

"The shortness of time at my disposal deprives me of the pleasure of making a careful investigation concerning this matter in order to be able to respond to your questions with exactness. I am not able therefore to answer these questions with mathematical precision, but I can, indeed, assure you (and this everyone here in Porto Rico knows) that the laboring capacity of our workingmen has notably increased to such a point, indeed, that an infinite number of laborers, completely invalidated by their anemia, and for this reason absent from their work in the plantations, are today performing work that cannot be surpassed in any place.

"There are two facts that speak with overwhelming eloquence for the value of the anemia campaign:

"1. That our production of sugar has been raised from 70,000 to 300,000 tons; the production of tobacco has increased surprisingly; and the coffee crops, with variations due to the rainfall, are now almost what they used to be before the cyclone of 1899. Moreover, there has not been any lack of personnel to handle the increased production.

"2. That in spite of the great number of laborers who descend to the coast, attracted by the work of the sugar and tobacco plantations, they are not missed in the mountain districts of the interior where coffee is cultivated and where the scourge of anemia was greatest.

"In short I believe that everyone here admits, as a fact beyond discussion, that the campaign against anemia has powerfully influenced the increase in the laboring capacity of our working people, those who have been treated being today as strong as the strongest. The important proposition now would be that government and planter should work together, each in his sphere of action, not only to prevent the disease from invaliding as before our country people, but to safeguard those who have been already cured against a reinfection, in order that the fecund work which you and your confrères have done may not be rendered sterile.

"With my best regards, I am, yours truly,
(Signed) X. MARIANI."

(Translation from Spanish.)

When we confront this data with our estimate in 1902, that 90 per cent. of the rural population and some less of the towns were infected with *Necator Americanus*, and that 70 per cent. of these were more or less sick, it will be seen that this estimate was not far from the truth.

We considered that we had to deal with about 800,000 infected at the beginning of our campaign when the population was 950,000; 300,000 were treated in the six years of existence of the special anemia service, four years of which that service consisted of Porto Rican physicians, under the direction of Dr. Pedro Gutierrez. From 100,000 to 200,000 more have received treatment to date, which have not been included in our official statistics, and 300,000 still require it. But of this 300,000, fully 200,000 are really light cases, or simply worm-carriers, leaving only about 100,000 who are palpably sick. The majority of these sick are in the hitherto inaccessible mountain barriers.

It is a natural temptation to figure out the millions saved per year to employer and employed; the value of lives which would have otherwise been lost; the impetus which agricultural life has received by raising the hemoglobin of the laboring poor of Porto Rico, but I will leave that to each one who hears or reads this narrative to estimate for himself.

Enough has been said to bring to the consciousness of everyone that scientific medicine has made a whole people 50 per cent. better physically than they were before, and has played a winning card in bringing about a 400 per cent. increase in Porto Rico's commerce.

URTICARIA TREATED WITH EPINEPHRIN.

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IN six cases of urticaria which I have treated by the subcutaneous administration of epinephrin the injections were followed by a rapid disappearance of the erythema and wheals.¹ In each case a dose corresponding to about eight minims for an adult of one hundred and forty pounds was given hypodermically, and the dose was repeated in ten minutes. Two doses sufficed in every instance to cause the complete fading of the rash. An improvement was usually evident eight minutes after the initial dose, and was most marked between ten and twenty minutes, during which time, especially in the severe cases, the rapidity with which the eruption subsided was very striking. After twenty minutes there usually remained some erythematous blotches, or small, pale wheals, which continued to fade until the skin looked entirely normal. All itching ceased in from five to twenty minutes after the first dose.

In Case V the eruption did not return until three days later, when epinephrin was again given (see Case VI). In Case II it recurred after seven hours. In the three most severe cases (Cases III, IV, and VI), all of which were serum rashes, the wheals began to reappear in from one to two and a half hours after the initial dose of epinephrin, and increased steadily for from one to three hours more, when the eruption was again at its height. I have no record of Case I, and cannot say whether or not the wheals recurred.

Unfortunately I was not able to be with any of the patients when the rash began to reappear, and therefore had no opportunity of repeating the treatment in such cases. There is no doubt that if the exciting cause of the urticaria is still sufficiently active the wheals will recur in an hour or two unless the treatment is continued. It will be interesting to see whether or not the condition can be relieved for longer periods, or even permanently, by repeated and properly regulated doses.

A brief account of each case follows. For blood pressure curves, see chart, page 376.

CASE I.—Boy, aged about twelve years, who while a hospital patient incidentally developed moderate urticaria, supposed to be of gastro-intestinal origin. He was given two subcutaneous injections of adrenalin ten minutes apart. The wheals started to fade

¹ The preparation used was the 1 to 1000 adrenalin chloride solution of Parke, Davis & Co.
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soon after the first injection, and rapidly disappeared after the second. I have no records of this case, and cannot say whether or not the wheals returned.

CASE II.—Man, aged twenty-eight years, who for some time had had two or three attacks every year of swelling and redness of the fingers and toes, generally but not always associated with urticaria. When seen by me he had many small wheals and irregular red blotches on the dorsum of both hands and wrists, and complained of a disagreeable sensation of swollen feet, which on walking were somewhat painful, and made him feel as if his shoes were full of cotton. The systolic blood pressure was 113 mm. He was given eight minims of adrenalin solution subcutaneously, and the dose was repeated in ten minutes. Eight minutes after the first dose the subjective sensations in his feet were less marked, and the wheals and blotches on both hands and wrists were fading. In twenty minutes only a few faint red blotches on his left hand remained, and one foot felt slightly swollen. In thirty-two minutes no trace of the eruption remained and both feet felt entirely normal. The patient remained well for seven hours, when the condition returned less severely than before.

CASE III. (Diphtheria).—Boy, aged three and a half years. Weight about thirty-five pounds. Systolic blood pressure, 75 mm. The patient had received a single dose of antitoxin eight days before. At this time his abdomen and the inner sides of both thighs were covered with large wheals, around which was a fiery red erythema. Wheals and red blotches were scattered irregularly over his face and both arms, and there was some edema of the foreskin. The eruption was a severe one, and the itching was extreme. Two minims of adrenalin solution were given subcutaneously, and repeated in ten minutes. In six minutes after the first dose there was a slight diminution of the erythema on his abdomen. In eight minutes a change on his abdomen, face, and thighs was perfectly distinct. In twelve minutes the erythema was nearly gone. The wheals then began to disappear with great rapidity, and in nineteen minutes had entirely faded from the face, abdomen, and right arm, a few still remaining on the left hand and thighs. These continued to fade, and in twenty-eight minutes had disappeared from his hand and right thigh, leaving only a few small whitish elevations on the inner side of the left thigh, which failed to entirely disappear. The edema of the foreskin was also gone. The boy was much relieved for the time being, and for the first time that day went to sleep. One hour and ten minutes after the first dose the wheals began to reappear, and three hours later were as bad as ever.

CASE IV. (Convalescent Diphtheria).—Boy, aged ten years. Weight about seventy pounds. Systolic blood pressure, 80 mm. 10,000 units of antitoxin had been given eight days before. Again

in this case the urticaria was severe, wheals and erythema being profusely scattered over the face, neck, calves, and arms. There were a few wheals on the abdomen, and the penis was swollen on one side. He was given four minims of adrenalin solution, and after ten minutes, five minims. Nine minutes after the initial dose there was slight fading on his neck, back, and right calf. Though the eruption was still very marked, the boy said there was no longer any itching. In fifteen minutes the eruption was rapidly fading, and in nineteen minutes was almost gone from the face, neck, and back. In twenty-five minutes the wheals were entirely gone, and all that remained of the eruption was a blotchy erythema, which still persisted on the right arm and both calves. These spots continued to fade, and in thirty-five minutes the skin was entirely clear. In two hours and a half after the first dose of adrenalin the wheals were again appearing, and soon after the eruption was as profuse as ever.

CASE V. (Diphtheria).—Boy, aged seven years. Weight about sixty pounds. Blood pressure, 80 mm. The patient had received 10,000 units of antitoxin, and had developed the eruption three hours later. When I saw him, one hour after the first appearance of the rash, there were a few single wheals on the left hip, face, shoulder, and pubis. The right cheek was swollen and blotchy. The rash was of a mild type. Four minims of adrenalin solution were given, and the dose repeated in fifteen minutes. In four minutes the wheal on his hip was distinctly blanched. In eight minutes all the wheals had faded somewhat. In sixteen minutes they were nearly gone. In twenty-five minutes they had entirely disappeared. The eruption did not return for three days, when it recurred in severer form, and the patient was again treated with epinephrin as Case VI. It is interesting to note that in this case the blood pressure failed to rise more than 2 mm., and yet the wheals were affected as in the other cases.

CASE VI.—Same boy as Case V, three days later. The eruption was much more extensive this time, the wheals covering in a solid mass the inner sides of both thighs, and being scattered over the face, back, and chest. The systolic blood pressure was now 68 mm. He was given four minims of adrenalin solution, and the dose was repeated in ten minutes. Slight fading was noticeable ten minutes after the initial dose. In nineteen minutes the face and back were entirely clear, the chest nearly so, and the thighs much improved. In thirty-five minutes the eruption had entirely vanished, except for a few small whitish elevations on the inner side of the left thigh, resembling those in Case III. These continued to fade, and fifteen minutes later were entirely gone. In two hours after the initial dose a few large wheals began to reappear on the back, and an hour and a quarter later the eruption was again at its height.

The striking manner in which the erythema and wheals have subsided in these cases is interesting in connection with work recently done on epinephrin by Janeway and Park.² Using strips of excised peripheral arteries they confirmed the work of Meyer³ and others, which showed that contraction occurred when subjected to epinephrin in high dilutions, and they showed further that the degree of contraction depended not only on the

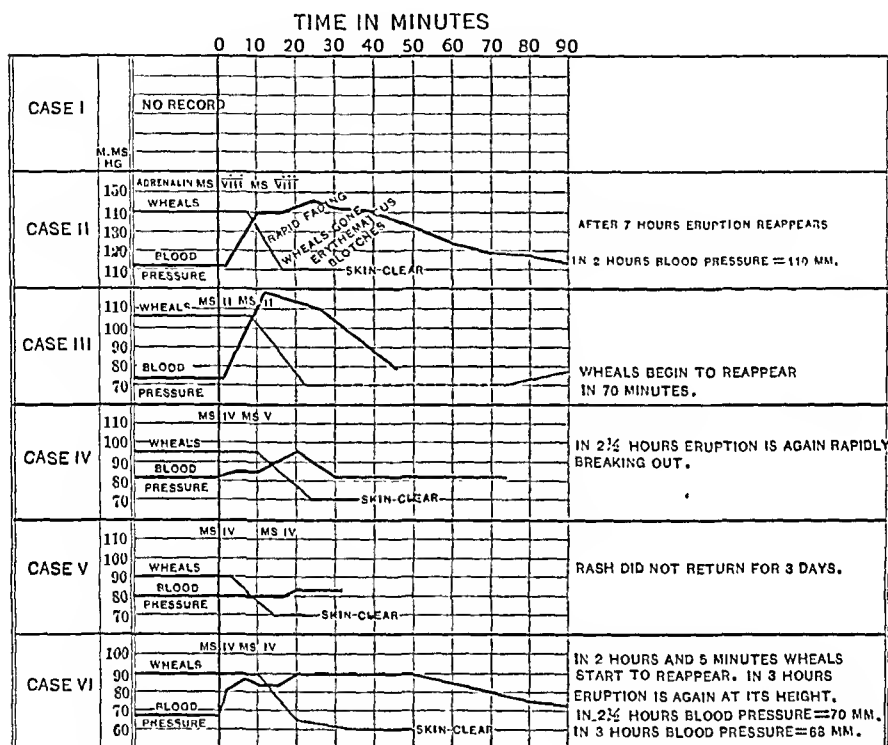


CHART.—The subsidence of the rash and its relation to the blood pressure. The heavy line represents the systolic blood pressure. The light line represents the eruption. When declining it indicates fading of the wheals. The point where it reaches the base line marks the time when the wheals have disappeared and only erythematous blotches remain.

strength of epinephrin, but also on the state of tonus in which the vessels were at the time. That is, if the vessels were already somewhat contracted, little further contraction resulted from the epinephrin; whereas, if they were relaxed, the contraction was much greater. Park⁴ found that the same principle held good in regard to the dilatation of the coronary artery of the ox, which is produced by epinephrin, and that if the artery were contracted

² The Question of Epinephrin in the Circulation and its Relation to Blood Pressure, Jour. Exper. Med., 1912, xvi, 541.

³ Ueber einige Eigenschaften der Gefäßmuskulatur mit besonderer Berücksichtigung der Adrenalinwirkung, Zeitschr. f. Biol., 1906, xlviii, 352.

⁴ Observations with Regard to the Action of Epinephrin on the Coronary Artery, Jour. Exper. Med., 1912, xvi, 532.

a much greater dilatation occurred than if it were already in a state of relaxation. He suggested that this might explain the striking relief often produced by epinephrin in cases of bronchial asthma, where the effect on the bronchi is out of all proportion to any apparent effect elsewhere in the body; for as has been observed by Eppinger and Hess,⁵ and also by Frank⁶ there may result marked relaxation of the bronchi, with little or no rise in blood pressure. In such cases as Park⁷ pointed out, the drug seems to have a more or less selective action on certain structures, depending probably upon their state of tonus.

From the results obtained in these six cases of urticaria, it seems probable that in such cases too the vessels in the wheals are in a state of optimal tonus for the action of epinephrin, and that on them the drug has an unusual and selective effect. In contrast to asthma, however, the rise of blood pressure which occurred was in most cases greater than usually follows subcutaneous injections of epinephrin in other types of disease, or in health, and may have been due to a generally relaxed condition of the arterial tree, which one would expect to be present in such cases. A relationship between the rise in pressure and the subsidence of the eruption is shown in the chart, where it is readily seen that in every instance except in Case V the wheals began to fade soon after a marked rise in pressure had occurred, and continued to fade while the pressure was rising or still above normal. On the other hand, the inconstancy of this relationship is shown in Case V, where the rash nearly disappeared before any rise of blood pressure took place, and by the fact that in most of the cases the wheals did not reappear for some time after the pressure had again fallen to its starting point. It is therefore by no means certain whether the disappearance of the rash depends entirely upon the local contraction of the bloodvessels or whether it also depends in part upon some other process. Meltzer and Auer⁸ have shown by animal experimentation that epinephrin retards absorption from the tissues into the blood and transudation from the blood into the tissues, and that this effect is maintained well after the blood pressure has fallen to normal. It is possible that this may be instrumental in causing the wheals to disappear, though it would seem more logically to be a factor in preventing their reappearance.

The effect produced in these cases of urticaria suggests that epinephrin might be used to advantage in certain more serious yet similar conditions. One such condition is "angioneurotic edema" in its various forms. At the present time, except for

⁵ Zur Pathologie des Vegetativen Nervensystems, Zeitschr. f. klin. Med., 1909, lxxvii, 344.

⁶ Bestehen Beziehungen zwischen chromaffinem System und der chronischen Hypertonie des Menschen, Deutsch. Arch. f. klin. Med., 1911, ciii, 397.

⁷ The Physiologic Action of Epinephrin on the Bronchi, Jour. Exper. Med., 1912, xvi, 558.

⁸ The Influence of Suprarenal Extract upon Absorption and Transudation, Philadelphia, 1904, xxvii, p. 8. Reported in Trans. Assoc. Amer. Phys., 1904.

general hygienic management, little can be done for these cases, and it will be interesting to see what can be accomplished with repeated doses of epinephrin. In cases of edema of the epiglottis or larynx due to disturbance of this type epinephrin given intravenously, if its action were similar to what it has been in these cases of urticaria, might well be the means of saving life, when the local application of the drug and other measures had failed.

Another such condition is anaphylaxis, with severe bronchial spasm and edema. From its physiological action on the bronchi and peripheral vessels, epinephrin should theoretically be the most specific of any drug in these cases. That it may relieve the asthma of anaphylaxis, at least temporarily, is well known to clinicians, and its effect on certain urticarias of this type has been shown in this paper. Whether or not it could be made beneficial in every such case if the doses were properly manipulated is a question of some interest. I know of one extreme case of anaphylaxis with dyspnea, but without edema, where epinephrin had no apparent effect, though it is impossible to say what larger and more frequent doses might have done. We know too little, however, of the possible reactions which may in turn follow the primary dilatation produced by the epinephrin to give more than moderate doses in such grave cases, and this point requires further investigation.

The rapidity with which the erythema has faded in my cases suggests the possibility of using epinephrin to differentiate rashes of purely vasomotor origin from those of other types. Hayes⁹ suggested its use in diagnosing serum erythema from the rash of scarlet fever. We have not yet had an opportunity of trying it in a case of scarlet fever, but it is rational to expect that the scarlet rash would fade but little or not at all.

In concluding, I wish to thank Dr. Joseph E. Winters, whose kind permission to work in his wards at the Willard Parker Hospital enabled me to obtain the cases of serum urticaria, and also Dr. R. Hayes for many courtesies extended to me while there.

THE DISSEMINATION AND PREVENTION OF YELLOW FEVER.

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IN order to avoid possible misunderstandings, I shall not enter into an argument regarding the relative merits of the observations of Beauperthuy, Knott, and others, but no discussion of

⁹ Personal communication.

this subject would be fair unless it embodied the credit which is due to Carlos Finley for arraiguing the stegomyia as the cause in the dissemination of yellow fever, and which did not recall the wonderful clinical observations of Carter in the Mississippi outbreak of 1898, in which he noted the apparent discrepancy between the incubative periods of the first secondary case in a house and those following it. This is true, because the notes of these two men were the most important factors in leading the United States Commission under Reed to pursue the proper line of research from the start.

To that commission, Reed, Carroll, Lazear, and Agramonte, we owe the definite, conclusive, and irrefrangible proof that the female *Stegomyia calopus* is the transmitter of yellow fever from man to man; that she receives her infection during the first three days of the man's illness and does not herself become dynamic for evil short of ten or twelve days, and the further proof that the mosquito is the sole means for such transmission, though naturally we cannot positively say that some other of this genus may not also transmit the disease until all have been tried. It is superfluous to recite the findings of this commission, as they are known to the whole world; but because there has been some inclination shown to still believe in the transmission of the disease by fomites, I think it well to report additional facts coming under my own observation, and bearing on this phase of the matter.

During the 1905 epidemic in New Orleans I arranged that all of our prophylaxis should be based upon the findings of the Reed Commission, and, pursuant to this policy, our yellow fever hospital was screened at every opening so effectively that no mosquitoes could effect an entrance. Only one portal was provided for entrance and exit, which was fitted with triple doors, two strong electric fans blowing outward day and night, and a boy stood in the vestibule to locate and destroy any chance entrant.

All fomites, soiled bedlinen, and clothing stained with vomitus, fecal matter, and blood from over 300 patients suffering from yellow fever, was carried without any disinfection to one of the benevolent institutions of the city, where it was laundered; and this was the only institution in the city which was free from yellow fever during the epidemic of 1905.

Our hospital, containing 120 beds, was manned as to medical staff, nurses, cooks, waiters, scullions, etc., with absolute disregard for the question of immunity, and no member of the personnel became infected, save one young woman, who subsequently confessed she had violated her obligations, and had slept one night outside in what was afterward proved beyond doubt to be an infected house.

Patients were permitted to be seen by friends and relatives, and sometimes whole families were taken into the hospital and

held under observation while one of their number was sick with yellow fever and their house was being fumigated, nor was there reason to suspect that infection was transmitted in this manner.

From the evidence of the commission, and from my own observation in connection with this hospital and with three or four epidemics, it appears to me there is no reason to believe that there is any other means of transmission save through the female *stegomyia* which has bitten an infected person during the first seventy-two hours of his fever.

The disease presents itself in what has been arbitrarily classified as endemic and epidemic form.

The endemic existence of yellow fever depends upon two factors: (1) The constant presence of mosquitoes of the genus *stegomyia*, and (2) the presence of a constant supply of non-immune material (people). The latter factor is supplied in two ways: one by population sufficiently large that its birth rate will supply the non-immune material, as is the case in such cities as Habana or Rio Janeiro, and the other by the steady incoming to a smaller town of people from remote places of habitation, such as is the case in communities like Cartagena, where the "paesanos," bringing Tagua nuts, are constantly arriving, resting a few days, and going home. Such cities as Guayaquil and Vera Cruz may supply both conditions.

The *Stegomyia calopus* is according to my observation entirely a domestic mosquito, and while I would not assert that under such conditions as might annihilate all human habitation near by that it might not breed in natural pools, it is nevertheless true that as matters ordinarily exist it always breeds in artificial water containers, such as cisterns, barrels, tubs, buckets, broken bottles, cans, stagnant drains with brick, stone, or cement sides, etc. It seems instinctively to avoid water courses having weeds and grass around their margin, and in a conversation on this subject with H. W. Thomas, of Manaos, I learned that the one breeding place known to him which was not deemed artificial, fulfilled artificial conditions in that it was a cleft in rock and free from vegetation.

Howard also states that the *stegomyia* gives evidence in its method of attack of long acquaintance with man, since it always attacks from the rear or under the lower edge of a garment, and never where it can be easily destroyed. He considers it almost as much domesticated as the barnyard fowl. Many have confirmed Howard's findings in this respect, also in regard to its habit of, biting at twilight after it has become accustomed to blood feeding, though prior to that time it is not so discriminating.

In 1905 I called the attention of Sir Rubert Boyce to the domestic character of this mosquito, and found him somewhat incredulous regarding my statement that I had never found it in any water containers save artificial ones; but I had the pleasure some months

later of meeting Dr. Boyce on his return from Central America and the West Indies, where he had verified my observations, failing to find the stegomyia in crab-holes and other natural pools.

This is *a propos* in connection with the statement of J. De Goyon¹ regarding French West African work. He states that much attention was paid to crab-holes, that vast numbers of them along the coast offer protection to the mosquitoes, and without noticing the apparent discrepancy, and almost in immediate connection says: "Le Moal has shown that the mosquitoes which inhabit crab-holes were principally *Catageiomyia senegalensis* and *Uranotænia annulata*." He then continues: "The larvæ found in odd water receptacles almost exclusively belonged to the genus stegomyia." He calls attention to the danger from non-reported cases, and advises a change in the manner of house construction, gutters, etc. All his observations are excellent, but he fails to note that poorly constructed wooden roofs and gutters furnish excellent breeding places.

K. S. Wise² also notes that "*Stegomyia fasciata* and *Culex fatigans* were found only in close proximity to human habitations. . . . The larvæ of stegomyia were never present in trenches nor unoccupied ponds." This corresponds with my observations stated at the 1905 meeting of the American Society for the Advancement of Science.

Wise also states that the anophelines breed in trenches overgrown with vegetation, in hollow stumps, etc., and that clearing arrests such breeding; these facts are pertinent to this discussion, because malaria tends to confuse diagnosis, and efforts should be made to eradicate malaria coincidentally with yellow fever.

The question of the flying radius of the stegomyia has given rise to much discussion, and for that reason I would submit some further observations of my own bearing thereon.

During July, August, and September, 1905, the old French quarter of New Orleans known as the Vieux Carré was the most pronouncedly infected section of the city.

The Louisville and Nashville Railroad runs through the river side of this section to its passenger station at the head of Canal Street. I purposely permitted unscreened passenger trains of this line to go out every day, with every seat full of passengers bound through to the North, and these trains were boarded at the Mississippi-Louisiana State line by young guardsmen of the Mississippi State Guard, all of whom were non-immune, who rode in the coaches across the whole State of Mississippi with passengers to the Alabama State line, where Alabama men took up the task of seeing that these passengers did not debark in infected territory.

¹ Revue Scientifique, September 23, 1911.

² Annals of Tropical Medicine and Hygiene, December 30, 1911.

I did this because there was no place where these ears would come within less than fifty yards of a dwelling house, and that no *stegomyia* from an infected room would fly fifty yards in the open sunshine. The result showed that my surmise was well-founded, as there was not a case of any kind of fever among these guardsmen, while there undoubtedly would have been had any infected mosquitoes been in the coaches. Naturally the coaches would have been fumigated had any illness occurred.

Again, on Burgundy Street, a long, low house, the middle one of three just alike, with windows of each exactly opposite those of the others, mostly open, and not more than fifteen to twenty feet between the houses, became infected, and so remained for about thirty-five days before it was discovered that every member of the family had the disease. Neither the neighbors to the right nor to the left visited this house, and neither did any of them contract the fever, though other people who lived at a distance who did visit the house became ill of yellow fever.

I am quoted by Rosenau as saying in 1898 that yellow fever never crossed the street save on a pair of shoes, and I am now even more convinced of the almost unfailing rule that to become infected with yellow fever one must enter a room, with a dim light, where yellow fever has been at least fifteen days before.

It is not to be denied that an infected mosquito might be imprisoned in a bag or piece of furniture and carried to some distant point *nolens volens*, but the contingency is so remote as not to be worth discussion.

It is unfortunate that so much of our work must depend upon deductive reasoning rather than facts, but it is nevertheless true, and for this reason I have submitted so much of this data.

In the sick-room the infected blood-feeding *stegomyia* finds all the congenial conditions of shade, blood, moisture, rest, and sunshine, and remains there, having practically changed her whole life habit since she tasted human blood; and, so far as my observation goes, she will never leave there unless the sick-room be entirely abandoned and left without even water, as happened in one instance in Baton Rouge, where an obscure case was traced to the fact that the patient slept in an open bay window, within ten feet of an old abandoned shack, where an Italian couple, who had fled from the New Orleans epidemic, camped for a week, during which time the man had a mild attack of yellow fever, and they then fled again, leaving their infected *stegomyiæ* behind them to infect the woman sleeping in the open bay window eighteen days later. This is the only case known to me where conditions would force the migration of the insect.

The prevention of yellow fever resolves itself naturally into: (1) The prevention of mosquitoes breeding, with the destruction where practicable of existing mosquitoes as a secondary phase; (2)

the isolation of the sick man, together with his infected mosquitoes and the final destruction of these infected mosquitoes.

The former proposition is one of interest in dealing with an endemic centre, and the latter is the one which comes to the fore in dealing with an acute outbreak demanding rapid and effective work.

In attempting to prevent breeding it is advisable to attack mosquitoes and their breeding grounds without regard for genus or species, because in so doing we shall answer the question, "May we not force the *stegomyia* into new breeding grounds, such as puddles, swamps, etc.," and again by attacking all mosquitoes we eliminate complications in the way of diagnosis, at least in part.

All ground within a quarter of a mile or more of the area to be treated should be reduced to ordinary dryness by drainage ditches and in the end by a system of subsoil drains, so that there will be no surface water to contend with, as ditches may pocket in places here and there and breed mosquitoes.

Thorough policing of the whole area not less frequently than once each week, and preferable once every five days, is essential, and is to be coupled with a clean-up of each water container, such as tin cans, broken bottles, etc., as well as grass and weeds in damp corners of the yard. All regular water containers, such as cisterns, barrels, buckets, tubs, fountains, church fonts, and cemetery urns, must be inspected at short intervals to see that they are not breeding mosquitoes, and to this end screens of eighteen meshes to the inch may be used on all containers, or a constantly renewed covering of refined petroleum may be applied to their surfaces. For the fountain a strong head of water and a number of small fish will suffice. The little minnows, known by the Jamaica negroes as "millions," serve this purpose. For the font, a tablet of bichloride or a small crystal of cupric sulphate, frequently renewed, is suggested, and the same rule will apply to urns, which I have seen swarming with *stegomyiæ*.

Experience has shown that the people will promise all these things and not do one of them, and that the paid lay inspector will attend to his duties so long as he is under the eye of the sanitarian.

Among the places to be watched as possible breeding grounds are the manholes of the city drainage and sewerage system, also the sagging roof gutter, which is a prolific source of danger, especially where shaded for most of the day. The remedy for the latter is simple: punch a hole in the dependent part with a ten-penny nail, unless it can be torn down entirely. The removal of all roof gutters, allowing the water to fall into paved ground drains and run freely away, is the ideal way to meet this question, and is the method adopted in the Canal Zone.

As to the destruction of existent mosquitoes of the genus *stego-*

myia, it is not impossible, as was proved in New Orleans, but is feasible only because of the habit of the *stegomyia* seeking dwelling with man, and making it therefore possible to destroy them by house fumigation; but such measures meet with objection in houses where there has been no fever, and it is possible that such work is better dispensed with in the interest of popular coöperation, where an endemic focus is being attacked and the work of necessity to be long continued.

In the handling of an epidemic, prompt and efficient work is necessary; this means the immediate isolation of every sick man and his accompanying mosquitoes; nor can this be too carefully done. We are confronted in this connection with the mild case in the negro and negroid, and to the cases on which it is sometimes difficult to obtain a report which we find among the younger members of the poorer class of whites unaccustomed to sending for a physician unless someone of the family is seriously ill. Two factors are predominant in these cases: (1) The ignorance of the class of the medical man usually employed by these people, and (2) the fact that these people, more than any others, object to the attentions of the health officer. It is therefore apparent that too much attention cannot be paid to the ignorant physician, to the slightly ill negro, nor to the young white child in similar case.

In dealing with the houses in which known or suspected cases of yellow fever have been discovered, it was my custom first to see whether the house had been properly screened with eighteen-mesh-to-the-inch wire cloth, and if not, to have screening done promptly, using mosquito netting as a substitute for wire cloth, and having the sick-room itself, as a double precaution, screened from the remainder of the house. The sick-room door can be easily screened by tacking two ample widths of the netting to the top and sides of the door, and attaching a wooden rod to the bottom of each width, so that the ends projecting into the door are higher than those at the side, resulting in the rod dropping into place and pulling the folds together immediately behind anyone passing through. With Guiteras I believe in careful screening, and in covering all cracks around the sick-room; also in the quietness with which this work is done, to prevent disturbing either patient or mosquito. The sick-room window should be screened from a ladder on the outside of the window. In order to prevent escape or entrance through the chimney, a cap should be placed on the top; or failing in this, some loose paper should be burned in the fireplace, with a little petroleum to make a rapid flame, and the front of the fireplace covered with a screen of wire netting.

After the patient is in condition to be removed to another room or house, three days having elapsed since he became ill, he is removed and every crack pasted over into which an insect may hide, and all drawers opened, so that the fumigant used may reach

all places in the room, care being taken that no mosquitoes are shut between the outside screen and the window in closing it. The room and its contents are subjected to either sulphur dioxide or cyanide, burning pyrethrum powder or any other fumigant. The whole house is simultaneously treated in the same fashion if the patient can be removed to another house. Otherwise we must treat part at a time with more than usual care.

I have never deemed it necessary to fumigate detached neighboring houses, but I consider a contiguous and connecting house to all intents and purposes, from a sanitary viewpoint, a part of the infected house, and treat it accordingly.

On August 8, 1905, I undertook, at the request of the Governor of Louisiana and the Mayor of New Orleans, to eliminate an existent epidemic of yellow fever in New Orleans, which had presented to that time 600 known cases, scattered over forty-four square miles of territory, among a population of 335,000, and with many indeterminate foci.

I deemed it necessary, under these conditions, to make an attack on all mosquitoes in addition to killing all infected *stegomyia*. The result was the total elimination of all yellow fever, nearly all *stegomyia*, and most of the anophelines and culicidæ by the end of October.

The work was continued for one hundred days from its inception, and the amount expended in round figures was from all sources \$325,000, a fraction under one cent per capita per diem.

We expended about \$50,000 for hospital equipment and maintenance, and \$75,000 for special treatment of infected houses, leaving \$200,000 for the total cost of one hundred days of elimination work, such as would be done in an endemic centre, with permanent eradication in view and which includes the overhead charges for all the work, being therefore a more than ample estimate of the cost for this latter class of work. Making allowance for slight inaccuracies in such calculations, the cost of such work would average from six to eight mills per capita per diem—less perhaps in large cities, and more in small towns on account of undue weight of overhead charges in the latter.

The endemic centre has been destroyed at Habana by Gorgas, and later a reestablishment of endemicity prevented by Juan Guiteras. The same thing has been done at Rio by Cruz, at Panama by Gorgas, and at Vera Cruz by Liceaga; and it cannot be doubted that the consistent application to all endemic centres of the kind of work above described will destroy endemicity in the whole world, and as epidemics are dependent on endemic seed beds for their existence, yellow fever will cease to exist, and Pasteur's postulate that it is possible to eliminate infectious diseases entirely can be demonstrated in this one.

CONCLUSIONS. The mosquito is the only disseminator of yellow fever, and the female *stegomyia* the only genus and species proved to be the carrier.

Yellow fever is only infective during the first three days of the attack, and the mosquito biting a patient after that time receives no infection.

The *stegomyia* itself cannot convey the infection to another human until after the lapse of at least ten days subsequent to the ingestion of yellow fever blood.

One attack of yellow fever generally gives immunity—not always.

Feeble susceptibility in the negro is sometimes confused with immunity.

Mild cases are the rule with that race, and this causes many cases to be overlooked.

Destruction of all breeding places for all varieties of mosquitoes, and especially *stegomyiæ*, *anophelines*, and *eulicidæ*, is necessary in dealing with endemic foci.

Rapid anti-epidemic work may be confined to destruction of infected *stegomyiæ* alone; but this is short-sighted.

THE SANATORIUM OF THE FUTURE.

BY HERBERT J. HALL, M.D.,

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THE introduction of more careful diagnosis and the decline of routine treatment, together with the gradual taking up of rational occupations and physical training, in the various sanatoria of the country has been slowly changing these institutions from rest cures in the extreme and objectionable sense to places of real reconstructive opportunity. The fact is that some of the most difficult and important cases of chronic illness cannot be adequately treated in the home, because of conflicting and unfavorable conditions, and because the physician does not have the opportunity to observe the patient or control his life for a sufficient length of time. The hospitals, as they are at present organized, cannot of course meet this requirement, so it seems probable that the sanatoria will become increasingly important as they improve their equipment.

But a great responsibility rests upon these institutions. They can no longer treat all their patients with baths and electricity. I believe they should, first of all, cease to be one-man places. No one man may hope to cope, single-handed, with all the perplexing

questions that the modern sanatorium must face. It seems reasonable that in the future these institutions will be situated near to great medical centres, so that while they give the advantages of country or seashore life they may call frequently into consultation the best men in the profession and in the different specialties. In the European countries the old-established spas may have their corps of physicians, highly trained and experienced in general medicine and in all the specialties. In this country it is too much to ask, at least for many years to come, that each sanatorium should have under its own roof specialists of the highest order; but it is not too much to ask that the best men should be kept in constant touch with such institutions and that their knowledge and experience should be frequently used for the benefit of the patients.

The sanatoria, wherever they are situated, will deal, of course, for the most part with the so-called nervous cases, because such illnesses almost invariably mean long periods of adjustment and reëducation even under favorable conditions. Fortunately modern medicine is coming gradually to a better understanding of the functional nervous illnesses, a better classification and a better treatment and a more serious consideration. The progress of psycho-analysis, for instance, and of the most excellent reëducative methods which are now in vogue bids fair to make clear many an obscure disability and to afford relief where relief might never have come.

Underlying the whole problem of successful management of any chronic illness, and concerning itself intimately with any kind of treatment, psychic, physiologic, or medicinal, is the question of the daily life of the individual—how it shall be lived that any treatment may have its best chances, and how it should be lived that routine and order may, in themselves, be reconstructive and educative.

I have for many years believed that the dependent and artificial life of the sanatoria, as well as the commonly difficult conditions of the home, represented, in the face of nervous or chronic illness, a serious handicap to any kind of treatment. I have believed that we might fatten the emaciated individual, that we might improve the anemia or the feebleness of any case of malnutrition and still leave the patient inadequate and helpless, unless we were able to supply, along with our cure, a training in actual living that would correct the evil effects of the habits of illness and leave the patient ready to meet with the maximum efficiency the requirements of ordinary life.

It would seem that the sanatorium of the future has a special opportunity in the training of the handicapped to meet easily, and so virtually to overcome, their limitations. In this connection I have for the last eight years been studying the possibilities of

the work element in sanatorium life, and I have arrived at certain interesting and suggestive conclusions. I have seen that in a good many cases of psycho-neurotic nature I can obtain satisfactory results by reorganizing the life of the individual by means of graded and progressive occupations. I do not mean by this that I have altogether neglected the ordinary therapeutic agents or that I have failed to consider or to treat such physical illness as may have been involved in my cases of nervous exhaustion, but the principal treatment has been that of adapting the individual to a systematic life of productive occupation, carefully planned to meet and not to exceed his capacity.

I have in many instances purposely neglected going into the subtleties of the individual outlook or into any attempt to correct, by direct advice, the faults of the undesirable habits, and I have seen many and many a mistaken idea, many a disabling excess or extravagance correct themselves, simply by virtue of the regular life and the normal conditions which the work cure, as I have carried it out, imposes. One reason why I have been glad to observe this is because I am, by nature, disinclined to the methods of psycho-analysis, and because I feel that I could not by such means accomplish the results which have been easy in this other way. No doubt many of my colleagues enjoy as little as I do long arguments and the continued study of mental processes. These men will be interested to know that the work cure is often a successful reconstructive measure.

I cannot, of course, say that this treatment, by itself, has been all sufficient in many psycho-neurotic cases, for inevitably other considerations have entered. Moreover, it is impossible to say how much or how little the physical treatment, which has been that of general practice, has availed. I cannot even say that my results are as good or even better than those of the usual sanatorium. Long experience and much classification and analysis alone can justify statements of results in chronic cases of any kind. There is so much chance of error that, in dealing with such indefinite conditions, we may never be able to make dogmatic statements. But if one may rely upon the improved morale of patients, and if we take increased efficiency as our standard of comparison, I believe that I may speak very favorably of the work cure.

In describing the work cure and its possibilities, I wish first of all to disclaim any desire or intention of making it a universal remedy or a cure-all. I have not gone far enough with it yet to know surely to what classes of cases it is best applied, or when it must not be used at all. But the experience of eight years has taught me that the application may be a wide one if we make it merely the background and basis of any physical or psychic treatment which may be indicated. And I believe that continued experi-

ence will make even clearer my conviction that there are many tedious cases of neurasthenia, complicated or not by physical conditions, which will yield to this method with practically no other means of treatment.¹

As I have described so fully at other times the technique employed,² I will only say now that the plan, as we have carried it out at Marblehead, involves sufficient housing and proper conditions of institutional life, leaving out for the most part the usual elaborate facilities for hydrotherapy and electrical treatment. It includes a reasonable diet planned for the average and rarely modified for the individual.³ It gives medicinal agents where these are manifestly needed; it supplies such amenities of life as may be found in music and in literary studies; it gives as much physical rest as seems required; it uses massage and physical exercises—these mostly corrective of the weak and relaxed physique of most nervous patients; it employs orthopedic corrective apparatus when the weakened muscles are unable of themselves to correct faulty carriage and the frequent condition of enteroptosis, and it gives work, not indiscriminately, but systematically, and in such measured doses as are indicated by the varying capacity of the individual.

Laying aside for a moment all physical considerations and all questions of mental or nervous complications, we must admit that most people are apt to be simple and happy when they are busy, and that they are almost sure to be complicated and involved when they are idle. I believe that a great many nervous patients fail to get well, and many organic invalids are made worse, because their lives have become disorganized from idleness and worry, as well as from pain, and that a long step will be taken toward a virtual cure when work within the capacity of the individual is made a part of the life.

The fatigue from which the subjects of nervous exhaustion suffer is one of the difficulties to be overcome. It can be overcome in most instances if the work, whatever its nature, is not pushed too hard, but is made so gradually progressive that there is never any strain or sudden effort required.

It should be easily possible to establish such industries in connection with the sanatoria and with most satisfactory results. I do not suppose for a moment that the usual sanatorium methods of treatment need be given up, for doubtless in some hands they are of the greatest use; but I believe that the sanatorium of the future

¹ I have had no experience with insanity, but I believe that work as a normalizer of life for these people promises excellent results and that the many institutions now proceeding along these lines will soon give valuable data.

² "Work Cure:" A Report of Five Years' Experience at an Institution Devoted to the Therapeutic Application of Manual Work, Jour. Amer. Med. Assoc., Jan. 1, 1910, liv, 12 to 14.

³ We do not, as a rule, treat here such conditions as diabetes or nephritis requiring special diets.

will in an increasing degree become a training school where people may at once simplify their lives and strengthen their hands.

It is of vital interest to know that we have been able to establish at Marblehead, workshops which are self-supporting from their own products.⁴ These shops are under the direction and constant supervision of skilled craftsmen, who accept the patients or pupils as assistants and apprentices. It is important to know that the system of occupation has proved a reconstructive and helpful measure in the lives of those who have overworked, quite as much as for those who have been too long idle. In these shops, haste is discouraged. Patience and reasonable care are at a premium. Because of the careful supervision and because of preparatory work by experts, the products of the pupils have always been of a high order.

The plan works as well for persons of means as it does for those without resources. The patient having an abundance of money may easily make use of the sanatorium and of the workshops to his advantage; but most of the private institutions of the present day are founded and conducted in such a way that the person of moderate or small means cannot obtain their advantages. It is easy to understand that many professional people, dependent as they oftentimes are upon salaries, and who would otherwise be seriously handicapped from lack of funds and from the unhappy consciousness that they were spending too much, may under this system, in favorable cases, be brought to a stage of productive efficiency which makes possible their maintenance and at the same time serves the interest of the institution. As is well known, many professional and business people break down nervously and become dependent. Business and the professions say to the worker: "If you can measure up to our standards, we will keep you employed and pay you a salary. If for any reason you are not able to meet the requirements of your position, you must go. We cannot use you further." The economic considerations of occupation for the handicapped are far reaching. We may some day see large producing organizations working on this basis, providing at least a livelihood for many people who would otherwise be helpless and dependent.

We have employed at Marblehead the crafts of hand-weaving, wood-working, metal-working, pottery-making, and cement construction. The power looms of the world are turning out their enormous products, and we cannot, of course, hope in the slightest degree to compete; but there are little possibilities which the power looms miss in the way of novelties in design and in weave which the hand looms may profitably and wisely pick up. This we have

⁴ We have recently moved into larger shops, so that at the present moment the industries are not quite self-supporting, but until this move the shops have for several years been on a paying basis.

shown many times. A design, for instance, for a small crib blanket having interesting and unusual patterns will for some months occupy our looms profitably. Meanwhile the designers must be considering another specialty to be ready as soon as the demand for the first design has ceased. Versatility in these lines is amply rewarded.

It must not be supposed for a moment that the untrained pupil can furnish these designs or prepare the looms for their weaving. But after a while the pupil may become so skilful in weaving that the products of his work amply justify the time and strength employed. Not infrequently a pupil may become proficient also in the most intricate and difficult parts of the work, becoming able to set up the looms and prepare them for unusual patterns.

The field of cement-working would, at first, seem to be an inhospitable one for such an institution. But, as a matter of fact, herein cleverness of management and design will count wonderfully. Cement-working, on a small scale, with carefully prepared moulds, is quite practical for untrained people, providing they are well directed. Cement, as everyone knows, is capable of a variety of excellent uses—first of all for building materials. The cement works are making quantities of tile and cement blocks, so far, unfortunately, mostly of crude design, and in the hopeless attempt to imitate stone.

After a year or more of experimenting we have discovered certain possibilities of color and texture in cement, which make it possible for us to produce brick and tile of unusual and attractive sorts, for which a fair price may be charged, and which can be made by hand better than in any other way. We are also making garden pots, garden seats, bird baths and the like in simple well-conceived designs, and which vary the monotony of the structural materials. We are even casting in cement small articles of special design for household or office use—such things as paper-weights, book-ends, ink-wells, pen-holders, etc. This is possible because the cement by special treatment is capable of a fine velvety finish, which makes it attractive, and because the color possibilities are greater than is commonly supposed.

It is in pottery-making that we have demonstrated most clearly the fact that practical industries may be founded upon the principles which we have outlined. We now have a pottery plant turning out a large and beautiful product, a pottery which is sold all over the country, and which has a large commercial field before it. This pottery is made by five people, two of whom were originally patients. Two of the others may well be called experts, and one of these has been under medical treatment part of the time, and owes his ability to earn a good living partly, at least, to the favorable conditions under which he works. Yet these five people produced in the last year and sold six thousand dollars' worth of

pottery, not a single piece of which was sold in any way except upon its merits, and in competition with other potteries on sale in various parts of the country. We do not often take new recruits into this department, because the work is of such a nature as to require careful handling.

Metal working I have tried with some persistence for a number of years, but I find that the physical exactions and the close work required make it, with difficulty, applicable to our special needs. I have also found it more difficult to sell the products.

Wood-working we have also tried persistently, especially wood-carving, and, while it is amusing and interesting, here also the close work seems to be more difficult to justify our using it indefinitely. Beautiful things may be made with the carving tools, but their sale is uncertain, and I do not recommend it as a craft for our special uses.

No doubt other men, with differing tastes and understanding, would make more of such things as metal-work and wood-carving, and perhaps use entirely different occupations. Of course, it must be understood that the success of any such work depends largely upon the enthusiasm and the skill of the directors and teachers. Without their cooperation and devotion to their work we could make no progress.

I shall hope as time goes on to develop a community of expert workers, partly recruited from among the patients and pupils, and producing goods of such quality as to command respect and interest anywhere, but depending for its life upon trained professional craftsmen. Into this atmosphere new pupils and patients may safely come, for it is a wholesome and hopeful atmosphere and one which can hardly fail to make a good background for the treatment of chronic illness of any sort, even of such kinds as do not allow of more than the slightest possible effort in the individual, because I believe that the happiness and development of those who are gaining and progressing under the system cannot fail to be contagious and inspiring. Here, as time goes by, we may develop conditions that will make such a community of the greatest human interest, and one which conserves in a large measure the faculties and abilities of many people who would otherwise have drifted on to all the unhappiness of chronic invalidism.

It is an amusing but suggestive fact that many people who are well are wont to remark, half in jest and half in earnest, after seeing the work which we are carrying on here, that they wish they might be just ill enough to warrant their coming into such a system which avoids so many of the complications and disappointments of the world outside, and yet which is no retreat, but rather a fair and reasonable meeting of the problems of life.

THE DIAGNOSIS OF THE FUNCTIONAL ACTIVITY OF THE PANCREATIC GLAND BY MEANS OF FERMENT ANALYSES OF THE DUODENAL CONTENTS AND OF THE STOOLS.¹

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THE voluminous literature of later years has included many studies dealing with the functional activity of the pancreas, and the methods in vogue for ascertaining the state of efficiency of this gland. Until recent years the function of this organ was roughly judged by the occurrence of such a symptom as glycosuria or the appearance of bulky and fatty stools. The attempt to utilize for diagnosis the external secretion of the pancreas, resulted in testing the stool for the ferments supposedly originating in this gland, or the urine for the same ferments. More recently a method introduced by Boldyreff and elaborated by Volhard has been employed. This method consists of introducing an olive-oil test meal into the stomach and testing for regurgitated pancreatic ferments the contents withdrawn.

It is at once apparent that no one of these methods is a direct one, for in every instance the pancreatic ferments are obtained only after dilution with other body fluids or after passage through other organs. Within the last few years, Einhorn,² Hemmeter,³ and Gross⁴ have independently suggested the use of a catheter or a soft rubber tube to be introduced into the duodenum and to directly collect the pancreatic secretion at the time of its discharge from its duct. These methods afford a means, which, if practical, avoid the numerous sources of error of the hitherto circuitous ways of collecting material for purposes of testing. The following paper is founded upon the results obtained by analysis of duodenal and stool ferments in 27 chosen cases. These cases were all chosen because of a particular interest attached to the external secretion of the pancreas. For comparison, the findings in the duodenum of a normal control are defined and tabulated.

METHOD OF OBTAINING DUODENAL MATERIAL. To obtain pancreatic secretion the Einhorn duodenal pump is used. This ingenious instrument was devised and perfected by Einhorn and has been used by him in many cases for collecting the duodenal contents. It consists of a vulcanized rubber catheter (one meter long) of narrow bore to one end of which is attached a small per-

¹ Read in part before the Eighth International Congress of Applied Chemists, September, 1912.

² Berl. klin. Woch., 1910, vol. xii, p. 522.

³ Arch. f. Verdauungs-Krankheiten, 1896, vol. ii.

⁴ Deutsch. med. Woch., 1909, xxxv, 706.

forated metallic capsule, and to the other end an aspirating glass syringe. My custom is to allow the patient to swallow the capsule and attached catheter (up to 80 centimeters) at eight o'clock at night, deglutition being assisted by the drinking of a little water. At twelve midnight, eight ounces of milk are drunk for the purpose of assisting the capsule to pass the pylorus during sleep. At 6.30 A.M. the same amount of milk is again administered. This latter milk serves as a test meal. Two and a half hours later the contents of the duodenum are aspirated. The catheter is slightly withdrawn until the point marked 80 centimeters is opposite the incisor teeth. At this point it is estimated that the capsule lies in the first part of the duodenum and opposite the point of exit of the pancreatic duct. Aspiration of the contents of the intestine is practised for five minutes, the volume and character of the resultant fluid being noted. This technique in all its steps, was adhered to rigorously throughout the course of this study.

The contents withdrawn are assumed to be duodenal contents if: (1) a radiograph showed the tube *in situ* in the duodenum; or, (2) if upon slowly withdrawing the tube, while aspirating, a distinct difference is noted between the contents obtained at the point marked 80 centimeters and the contents withdrawn after the metallic capsule is felt suddenly to enter the larger cavity of the stomach (56 centimeters). When the capsule lies in the duodenum, one obtains in the course of five minutes 10 to 40 cubic centimeters of golden-yellow, slightly acid or neutral, rather viscid fluid, with a more or less opalescent hue. This material can be aspirated only slowly. At first the contents present in the duodenum, 10 to 20 cubic centimeters, flow easily; then under continued negative pressure one obtains slowly, as it is secreted, a few cubic centimeters more of clearer golden yellow fluid. This material enters the aspirating syringe drop by drop, or rhythmically, every 20 to 30 seconds, with a rapid gush of 1 to 2 cubic centimeters of material. This latter phenomenon is probably due to a peristaltic acceleration of the secretions entering the duodenum at the moment and to the periodic expulsion of gastric juice.

The duodenal contents aspirated are almost always acid, due to the presence of the acid chyme, incompletely neutralized by the alkalinity of the pancreatic and biliary outflow. (The acidity was usually in normal cases 10 to 20 "acidity per cent.") The opalescence or milky appearance is similarly due to the expulsion through the pylorus of the incompletely digested milk (whey). When the capsule and catheter are withdrawn, until the former enters the stomach, a sudden gush of strongly acid milky material in great abundance is observed. This "retraction test," noted by Einhorn and by Hess⁵ (the latter employing a catheter in infants for the

⁵ Amer. Jour. Dis. Children, 1912, iii, 133 and 304.

purpose of obtaining duodenal juice) serves to differentiate duodenal from gastric contents, and is very important in cases where the biliary duct is obstructed, for here the absence of the golden bile in the duodenum complicates an otherwise simple maneuver.

CHEMICAL METHODS. Having obtained the contents of the first part of the duodenum, the presence and quantitative strength of the ferments is estimated. The fluid, after dilution with twice as much distilled water, was divided into two parts, one portion being kept acid (occasionally neutral), the other being made slightly alkaline with $\frac{n}{10}$ NaOH. The first portion serves for testing for amylase and lipase, the latter for the protease. The chemical methods as finally evolved are as follows:

1. **DUODENAL FLUID.** *Amylase.* In every one of several test tubes are placed one cubic centimeter of the fluid to be tested. Increasing amounts, from 0.5 c.c. to 6 c.c., of 1 per cent. starch solution⁶ (Kahlbaum's soluble starch) are added to the successive test tubes, and then water to bring the volume up to 10 c.c.; incubation proceeds at 40° C. for one hour. The material is then tested by adding Lugol's solution drop by drop until an excess of iodine is apparent. The last tube in the series which fails to react for starch is the tube from which the reading is taken. The number of cubic centimeter of starch solution in this test tube multiplied by the dilution (three) gives the factor accepted as representing the amylolytic activity of 1 c.c. of duodenal contents in one hour.

Lipase. To 10 c.c. of distilled water are added 1 c.c. of the diluted duodenal juice, 1 c.c. of ethyl butyrate, 1 c.c. of toluol, and a drop of 1 per cent. alcoholic phenolphthalein solution; the whole is then made exactly neutral with $\frac{n}{10}$ NaOH and the total amount of fluid brought up to 25 c.c. After stoppering the flask, it is shaken forcefully for fifteen seconds and again brought to the exact neutral point.

A control test was always prepared, the duodenal juice of the control being boiled actively for five minutes before addition to the flask.

After incubation for twenty-four hours at 40° C. the two flasks are titrated for free acid, and the amount necessary to bring the control to neutral subtracted from the free acid in the test flask. The result multiplied by three (the dilution of the duodenal juice) denotes the lipolytic strength of the test material.

Protease. To test for alkali protease, Mett tubes, coagulated egg-albumen cubes, Fermi gelatin tubes (5 per cent. and 10 per cent.), and casein (Gross-Fuld method, as suggested by them for use in stool tests) are utilized.

2. **STOOL.** A 4 to 50 dilution of stool⁷ in slightly alkaline distilled

⁶ Prepared fresh every week; thymol as preservative.

⁷ The diluted stool is used without being filtered, lest the strength of the ferments be attenuated in the process of filtration.

water is used as a basis for the estimations. The specimen of stool obtained is always a fresh specimen of that morning or a specimen obtained late during the night. No catharsis is used, as Ambard, Binet and Stadel⁸ have demonstrated the marked inconstancy of results following purgation.

Amylase. The Hawk⁹ modification of the Wohlgemuth method was adopted in a slightly different form.

Lipase and Protease. The same methods as employed in testing the duodenal contents are employed.

TECHNICAL DISCUSSION OF TESTS.

There are few universally accepted methods for quantitative ferment analysis. The technique of this branch of biological chemistry is still in the evolutionary stage, and there are hardly two workers who can agree on methods, or on the interpretation to be derived from similar methods. A few remarks on the technical considerations of the tests appear warranted.

1. THE METHOD OF OBTAINING THE DUODENAL CONTENTS. At first the method used was to insert the duodenal pump in the morning and withdraw the contents after three or four hours. But it was found in most instances that this interval was far too short to allow the capsule to be propelled through the pylorus, and even a period of five to six hours during the day was insufficient. But when the tube was swallowed in the evening and the patient put at rest through the night, it was very exceptional to find the capsule still in the stomach in the morning. This delay occurred in only two classes of cases, pyloric stenosis and pyloric spasm associated with ulcer or hyperacidity.

In all instances the fluid removed was divided into two parts, one remaining acid, the other being made slightly alkaline with NaOH, and was then immediately iced. The tests were carried out five hours later. It was ascertained that in estimating amyolytic power, it was necessary to preserve the duodenal juice acid. In neutral or alkaline juice it was noted that the amyolytic ferment had apparently disappeared, due probably to the presence of active trypsin. When the material was preserved in its original acid state, the amylase could be kept for twenty-four to forty-eight hours with practically no loss of strength.

2. IDENTITY OF THE AMYLOLYTIC FERMENT. The question that frequently arose was whether one was dealing in the duodenal contents with salivary amylase carried through the stomach into the duodenum or actually with the similar pancreatic ferment.

⁸ Compt. rend. Soc. d. Biol., 1907, p. 265.

⁹ Arch. Int. Med., 1911, viii, 552.

Numerous tests of the gastric contents obtained in the course of removing the tube from the duodenum (and allowed to stand the usual five hours before testing) showed an absence of active amylase or only the slightest trace of this enzyme. So that it seems fair to assume that salivary amylase under these conditions, is destroyed by the presence of active pepsin, but that the pancreatic enzyme, even in the presence of gastric acid and pepsin, maintains its activity even for many hours.

In an article by Ambard, Binet and Stadel,¹⁰ it was experimentally shown that the salivary amylase of the dog was only $\frac{1}{20}$ as strong as that of the pancreas; intestinal amylase only $\frac{1}{250}$ of the strength of pancreatic ferment. Extracts of the mucosa of the duodenum of dogs showed only the slightest amylolytic power, too faint to interfere with tests for pancreatic amylase. However, Roger¹¹ states that salivary amylase, even after its destruction by the gastric juice can augment pancreatic amylolytic activity, the "pouvoir zymotique" of the original ferment becoming a "pouvoir zymosthenique" after being acted upon by the gastric pepsin. It is very questionable whether this ability of the destroyed salivary enzyme is at any time sufficient to materially alter the figures obtained for pancreatic amylase.

3. PRESERVATION OF THE LIPOLYTIC FERMENT. With regard to lipase, it was similarly found that this ferment was best maintained in the acid duodenal contents, being apparently protected in this manner from the destructive activity of the trypsin. In neutral and alkaline material lipase was demonstrated only in very small amounts after the fluid had been iced.

4. PRESERVATION OF THE PROTEOLYTIC FERMENT. The activity of the alkali-protease was best maintained in alkaline fluid. While even in acid medium strong alkali-protease was demonstrable upon neutralization several hours later, yet this ferment was several times stronger in fluid maintained alkaline. The activity of the acid-protease (pepsin) in duodenal juice was not interfered with.

That autodigestion of pancreatic juice takes place very rapidly at high temperature has been convincingly shown by Nicolle and Pozerski.¹² These authors have demonstrated a very rapid weakening of all the ferments when the fluid is maintained at 50° C. Hence, the precaution of rapidly chilling the fluid when secured, is seen to be necessary in quantitative estimations of ferment strengths.

5. IDENTITY OF THE PROTEOLYTIC FERMENTS. To return to a consideration of the alkali-protease found in duodenal content, one must consider that we are dealing with two ferments: trypsin and erepsin. Erepsin originates from two sources, the duodenal mucosa (Cohnheim¹³) and from the pancreas (Bayliss and Star-

¹⁰ Loc cit.

¹¹ Archiv. de Malad. de l'Apparat Digest. et de la Nutrition, 1909, iii, 509.

¹² Ann. de l'Inst. Pasteur, 1911, xxv, 336.

¹³ Zeitsch. f. Phys. Chemie, No. 33, p. 451; No. 35, p. 134.

ling¹⁴). Schaeffer and Terroine,¹⁵ experimenting with the excretion of an artificial pancreatic fistula in the dog, showed that in fluid in which trypsinogen was present but not activated by enterokinase, an ereptic ferment with peptone splitting properties was still present. Of the tests for alkali-protease, neither the Mett tubes nor the coagulated egg-albumen cubes are attacked by erepsin; nor are the Fermi gelatin tubes digested by erepsin. To establish this latter point, three fresh extracts of duodenal mucous membranes containing active erepsin (one cat, one dog, and one human intestine) were prepared after the method of Cohnheim. None of these extracts liquified gelatin even after three days.

These same extracts in their most concentrated form were tested for the casein digesting power of the intestinal mucosa. That the digestive power of these intestinal extracts is only a very slight fraction of the same power of the pancreatic secretion is seen by a comparison of the results obtained. Thus cat mucosa extract in dilution of 1 to 15, dog mucosa extract 1 to 140, human mucosa extract 1 to 10 digested 10 c.c. of 0.1 per cent. casein solution; normal human duodenal contents containing pancreatic secretion digests the same amount of casein in dilution up to 1 to 10,000. It seems therefore fair to deduce that the amount of erepsin present both in the mucous membrane of the duodenum and in the pancreatic secretion could not account for the active proteolysis of casein as found in duodenal contents. Hence, we seem justified in assuming that the pancreatic trypsin is the active factor here, and erepsin, while unquestionably present, yet of little moment in the tests, as carried out.

A similar process of reasoning seems justified in discussing the results of the stool examinations; for if the concentrated extract of normal duodenal mucosa digests casein in dilution of only 1 to 10, how can we explain the proteolysis of casein in dilutions of the stool up to 1 to 10,000 or 1 to 20,000, as frequently found, except on the hypothesis that it is the much more powerful pancreatic trypsin that is appearing in the stool.

Frank and Schittenhelm,¹⁶ by means of complicated polypeptic splitting experiments, seem to demonstrate that the protease present in the stool is erepsin, rather than trypsin. It is difficult to harmonize their findings with such simple facts as the above. The occasional finding of a ferment in the stool which liquifies gelatin, would tend to confirm the impression that this ferment derives its origin from the pancreas. That bacteria do not simulate the results of the human ferments seems established by the fact

¹⁴ Jour. Phys., 1903, No. 30, p. 61.

¹⁵ Jour. de Phys. et de Path. Gén., 1910, xii, 884.

¹⁶ Zeitsch. f. Exp. Path. u. Therapie, 1910, viii, 237.

that a case in which the pancreatic ducts has been proved to be closed gave complete negative results in both duodenal and stool analyses.

RESULTS OF TESTS OF THE DUODENAL CONTENTS OF A NORMAL PERSON.

One male adult, apparently in perfect health, furnished repeated specimens of duodenal contents.

The results on the different days are tabulated as follows:

TABLE I.

Amylase:

March 21, 1 c.c. duodenal juice hydrolyzes	6	c.c. of 1 per cent. starch solution in one hour.
March 28, 1 c.c. duodenal juice hydrolyzes	6	c.c. of 1 per cent. starch solution in one hour.
May 13, 1 c.c. duodenal juice hydrolyzes	10	c.c. of 1 per cent. starch solution in one hour.
May 14, 1 c.c. duodenal juice hydrolyzes	9	c.c. of 1 per cent. starch solution in one hour.
May 18, 1 c.c. duodenal juice hydrolyzes	24	c.c. of 1 per cent. starch solution in one hour.
May 10, 1 c.c. duodenal juice hydrolyzes	30	c.c. of 1 per cent. starch solution in one hour.
Normal average = 14.1 c.c.		
Normal limits = 6-30 c.c.		

Lipase:

March 21, 1 c.c. duodenal contents require	3.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
March 28, 1 c.c. duodenal contents require	3.6	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 13, 1 c.c. duodenal contents require	0.6 ¹⁷	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 15, 1 c.c. duodenal contents require	0.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 18, 1 c.c. duodenal contents require	1.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 26, 1 c.c. duodenal contents require	0.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
Normal average = 1.96 c.c.		
Normal limits = 0.6 to 3.9 c.c.		

Alkali-protase. Casein test:

March 21, duodenal contents in dilution of 1 to	300	digests 10 c.c. of 1 per cent. casein solution.
March 28, duodenal contents in dilution of 1 to	3,000	digests 10 c.c. of 1 per cent. casein solution.
May 15, duodenal contents in dilution of 1 to	10,000	digests 10 c.c. of 1 per cent. casein solution.
May 18, duodenal contents in dilution of 1 to	400	digests 10 c.c. of 1 per cent. casein solution.
May 20, duodenal contents in dilution of 1 to	3,000	digests 10 c.c. of 1 per cent. casein solution.
May 21, duodenal contents in dilution of 1 to	1,000	digests 10 c.c. of 1 per cent. casein solution.
May 29, duodenal contents in dilution of 1 to	1,000	digests 10 c.c. of 1 per cent. casein solution.
Normal average = 1 to		2,666
Normal limits = 1 to		300 to 1 to 10,000

Other Tests:

	Fermi, twenty-four hours.	Gelatin tubes, forty-eight hours.	Mett tubes.	Albumin cubes,
March 21	3.5 mm.	6.0 mm.	2 mm.	Slight rounding.
March 28	8.0 mm.	11.0 mm.	1 mm.
May 18	Much digested
May 20	5.0 mm.	10.0 mm.	1 mm.	All digested
May 25	8.0 mm.	14.0 mm.
May 29	10.0 mm.	15.0 mm.
Normal average .	7.0 mm.	11.2 mm.		
Normal limits . .	3.5 to 10 mm.	6.0 to 15 mm.		

From a study of these tables it will readily be seen that quantitative estimates of the strength of pancreatic ferments obtained

¹⁷ On one occasion no lipase was demonstrable.

from the duodenum of a normal man vary within wide limits. In practically every instance the three ferments tested for are found, and found in an active state. In only one instance was one ferment (lipase) absent. When tested for, rennet was always found. There is no method, however, of deciding whether this was gastric rennet or possibly a similar ferment from the pancreas.

PATHOLOGICAL CASES.

With this study of a normal adult male as a basis, further studies were undertaken on cases of interest because of pathological conditions. The cases observed are grouped according to similarity of diagnosis. The results obtained are presented in the accompanying table, with remarks:

GROUP I. *Cases of Cholelithiasis.* In these cases, the diagnosis of which was confirmed by operation, the ferments in the duodenum were found in an active state. A fairly wide range of variation is observed, yet in general the ferments are either normal or hypernormal in their activity. The exception is Case V, examined before operation. Here the absence of amylase and lipase suggested some abnormality of pancreatic secretion; at operation the head of the gland was found swollen and infiltrated to a marked degree. Bile flowed freely into the duodenum in all these cases; occasional admixtures of the bile with heavy viscid mucus indicated a condition of catarrhal cholangitis or cholecystitis.

GROUP II. *A Case of Acute Pancreatitis.* This case was one of acute pancreatitis with a diffuse abscess involving the body of this organ. The pancreatic ferments in the duodenal content were absent except for a faint lipolytic ferment. The identical condition was found on examination of the stool. As the head of the pancreas was found at autopsy to be preserved and the duct patent, it seems reasonable to conclude that an acute inflammation and degeneration had involved the entire gland, the result being that the ferments were either not elaborated, or as in the case of lipase, secreted but feebly. The corresponding result in the stool is of interest.

GROUP III. *Cases of Obstructive Jaundice.* The question here involved was: Is the pancreatic duct open, and is the pancreas secreting or not? In the first two instances (Cases VII and VIII) the duct was evidently open and active pancreatic ferments entered the intestine. These cases were one of intra-abdominal new-growth with evident masses throughout the abdomen, and one of post-operative stricture of the bile ducts. It is evident that the pathological condition affected the common bile duct but did not interfere with the patency of the pancreatic duct or ducts. In either case if the main pancreatic duct was obstructed it is evident that the accessory duct of Santorini maintained full compensation.

TABLE II.

	Amount.	Reaction.	Bile.	Duodenal Contents.		Stool.							
				Amylase.	Lipase.	Casein.	Fermi.	Mett.	Cubes.	Amylase.	Lipase.	Casein.	Fermi.
Case I ¹³ Case II ¹³ Case III ¹³ Case IV ¹³ Case V ¹³	7 c.c. 15 c.c. 35 c.c. 10 c.c. 27 c.c.	Acid Acid Acid Neutral Acid	++ ++ ++ ++ ++	Group A. 10 c.c. 12 c.c. 30 c.c. 24 c.c. 0	0 6.3 10.0 3.6 0	1 to 5,800 1 to 12,000 1 to 1,000 1 to 18,000 1 to 5,000	— — 3 10 10	— — 0 10 —	— — 0 10 —	— — 0.1 0.25 —	— — 1 to 700 1 to 50,000 —	— — — 2 —	
Case VI ¹³	10 c.c.	Acid	+	Group B. 0	1.8	0	—	—	—	0	0.2	0	—
Case VII Case VIII ¹³ Case IX ¹³	12 c.c. 10 c.c. 10 c.c. 5 c.c.	Neutral Acid Acid Acid	0 0 0 +	Group C. 4 30 0 4	2.4 0 0.5 3.4	1 to 4,000 1 to 4,000 0 1 to 600	3 {3 5 — 3	0.5 — 0 0	— — — —	0 0.5 — 2	0.3 1.0 — 0	0 0 — 0	0 0 — 1 to 200
Case X Case XI	25 c.c. 50 c.c.	Neutral Acid	++ ++	Group D. 27 15	— 1.0	1 to 18,000 1 to 4,000	7 1	0 0	— —	8 —	1.5 —	1 to 3,000 —	0 —
Case XII Case XIII Case XIV	20 c.c. 8 c.c.	Acid Alkaline Acid	++ ++ +	Group E. 20 + 0	— — 0	1 to 6,000 + +	— — —	— — +	— — —	+ 0 {1.0 5.0	1.5 0 —	1 to 5,000 1 to 5,000 —	— — —
Case XV Case XVI Case XVII ¹³ Case XVIII	15 c.c. 3.5 c.c. 7 c.c. 4 c.c.	Acid Alkaline Acid Acid	++ ++ ++ ++	+ + + — 9 3	0 + + — 2.4 5.4 8.4	+ + + 0 1 to 1,400 0 1 to 4,000	— — 10 — 3	— — 0 0.5	— — — — 6.0	— — — — 0.1	— — — — 1 to 30,000	— — — — —	
Case XIX Case XX Case XXI	25 c.c. 9 c.c. 15 c.c.	Acid Acid Acid	++ ++ +	Group F. 6 9 30	4.5 12.6 2.7	+ + 1 to 4,000 1 to 6,000	— — {3 7	2 0 0	— — —	— — 1	— — 0	— — 1 to 700	— — —
Case XXII Case XXIII	3.5 c.c. 25 c.c.	Acid Acid Acid	++ ++ —	1.5 6 6	6.0 0 0.6	1 to 4,000 1 to 34 1 to 4,000	2.5 0 15	— — 1	— — +	8 — —	0.4 — —	0 — —	0 — —
Case XXIV	3 c.c.	Alkaline	+	1.5	1.2	1 to 500	{5 11	1 1	+	— 2.5	— 3	— 1 to 125	— —
Case XXV ¹³ Case XXVI ¹³	40 c.c. 12 c.c.	Acid Neutral	++ ++	Group G. 0 4	5.6 3.3	1 to 4,000 1 to 500	8 4	1 1.5	— —	— 10	— 0.15	— 1 to 1,700	— 0
Case XXVII	—	Group H. 0	0.6	1 to 12,000	—	—	—	—	—	—	—

¹³ Diagnosis confirmed by operation or autopsy.

In Case IX, on first examination the absence of all the ferments from the duodenum except a weak lipolytic ferment, and the absence of all the ferments from the stool, led to the diagnosis of complete pancreatic obstruction involving all the ducts emanating from the gland. On a second examination several weeks later, the results of both duodenal and stool analyses indicated some return of pancreatic ferments in the intestine. On autopsy, the head of the gland and the duodenum were found involved in a massive sarcomatous tumor. The ducts behind the new-growth were greatly dilated and distended with retained fluid. It seems probable that from time to time the pressure in the ducts was sufficiently great to force pancreatic secretion through the new-growth and into the intestine. This would seem the most likely interpretation of the later partial return of the characteristic ferments in the duodenum.

GROUP IV. *Cases of Hypertrophic Cirrhosis of the Liver.* Group IV represents the findings in two cases of hypertrophic cirrhosis of the liver. From the ferment analyses, the pancreas would seem to be secreting a fluid of high potentiality. The examination of the stool in the one case agrees with the findings in the duodenal material.

GROUP V. *Gastric Cases.* In this group is collected the data for various gastric diseases. As far as one can judge there is no evidence of disturbance of pancreatic secretion. It is of interest to note the absence of trypsin in a case of carcinoma of the stomach.

Case XVIII, one of achylia gastrica, requires a note. Repeated analyses of gastric contents showed the absence of both pepsin and rennin as well as all traces of acid. The pancreatic secretion is, however, active, all three of the ferments being present. Ehrman and Lederer,¹⁹ employing the Volhard test meal method, found an active pancreatic ferment (trypsin) in these cases. In the duodenal contents, however, obtained by me in this case, no rennin was demonstrable. The question of the presence of a milk-coagulating ferment secreted by the pancreas is still an open one. The only facts bearing on this point in the living person are presented by authors who have tested the secretion collected from pancreatic fistulae in diseased states. The results are contradictory; in a few instances a milk coagulating ferment being present, in others absent. With the direct method of collecting pancreatic secretion *via* the duodenum, no data on this point is at hand. In all instances with this means, some stomach contents are mixed with the duodenal fluid, and hence an individual test for pancreatic rennin is impossible. But in this instance gastric rennin, was repeatedly shown to be absent. Hence the inability to demonstrate in the duodenal material a milk coagulating ferment would speak for the absence of this enzyme in the secreting pancreatic

¹⁹ Berl. klin. Woch., 1908.

gland. It is hardly probable that the absence of the enzyme from the gastric contents would result in a similar suppression in the pancreas, since all the other ferments known to be present in pancreatic secretion were actively demonstrable, and unaffected by the gastric condition.

GROUP VI. *Cases of Diabetes Mellitus.* In general it may be said that these cases do not show any variation from normal figures, all the three ferments tested for being found present and active. In only one instance was the reaction for amylase weak (Case XXII). In the instance of Case XXIII, on a strictly limited milk diet, the ferments were all only feebly present. A later examination, on a more liberal diet (oatmeal and milk) revealed ferments of greater strength.

Case XXIV was of interest, being a case of diabetes mellitus in a female adult with a distinct history of cholelithiasis and abdominal attacks indicating pancreatitis. The stools in this case were bulky, grayish-white, and frequent. Metabolism studies indicated, even on a restricted diet, a loss in the stools of 54 per cent. of the fat, and 29.4 per cent. of the nitrogen intake, corroborating, so far as our studies of metabolism would indicate, pancreatic insufficiency.

The duodenal findings demonstrated a very scant secretion into the intestine, though of high potentiality. The stool in the same case showed active ferments, though only weak protease.

From the study of these cases it seems probable that the external secretion of the pancreas plays no role in the pathology of diabetes mellitus. This conclusion should not be interpreted to exclude the presence of a chronic pancreatitis with changes in the islands of Langerhans in these cases, for it can be conceived that these changes might be present and yet the external pancreatic secretion be uninfluenced, at least not demonstrable by our present methods. No idea of the internal secretion of this organ is obtainable from these analyses.

GROUPS VII AND VIII. *Miscellaneous Cases.* The ferments are present and active, except for amylase, which is absent in two instances. The failure to demonstrate this ferment was probably due to faulty technique in the early tests.

REMARKS. The original intention of this study was to determine (1) the limits of ferment activity in the normal duodenum; (2) possible variations from these normal limits in pathological cases; (3) to determine in how far the analysis of the ferments of the stool gave an indication of pancreatic functional activity.

In regard to establishing a standard for the strengths of the ferments as normally secreted, Table I represents the limits of variation. It would seem that the pancreatic ferments show fluctuations of strength from day to day even under identical conditions, but that such fluctuations may be said to be within reasonable bounds. However, the occasional failure to detect amyl-

ase or lipase in seemingly normal secretions must be noted. These ferments show the greatest variability in strength, and may apparently be occasionally absent. The protease is the most constant and is always present in the duodenum when the pancreatic duct is open. In spite of the arguments against casein as a test of trypsin alone, I would hold that erepsin, though present, is never sufficiently strong to interfere with the test as an index of pancreatic trypsin.

Of the pathological cases examined, the case of acute pancreatitis shows decided diminution in the activity of the pancreatic ferments. The pancreatic gland was found decidedly diseased at autopsy. In Case IX (the case of sarcoma of the duodenum) the ferments were absent from the duodenum on one occasion; also absent from the stool. The diagnosis of complete blocking of the ducts was confirmed at autopsy. In Case V, on account of the absence of two of the ferments from the duodenal juices, a disease of the pancreas was expected. At operation the duct was found patent, but the pancreatic gland was found swollen and inflamed.

In Case XXIV the metabolism studies indicated pancreatic disease. The ferments were found strongly present; the amount of secretion into the duodenum was, however, very scant.

The variability of the strength of these same ferments as tested in the stool is far greater than in the duodenum. The occasional absence of a ferment is a more frequent occurrence. In general where these enzyme are strongly present in the duodenum they are also demonstrable in the stool. The protease is here no longer reliable as an index of pancreatic trypsin. For in Cases VII, VIII and XXII, though a strong reaction for trypsin was obtained in the duodenal contents, this enzyme was not demonstrable in the stool (casein and gelatin tests). However, in Case IX, when the protease was absent from the duodenum, it was also absent from the stool; and when it reappeared in the former, it also reappeared, though weakly, in the latter. We may conclude that a positive test for trypsin in the stool signifies an open pancreatic duct; a negative test does not necessarily imply that active trypsin is no longer being secreted into the duodenum.

The important question that rises is: Can this method of estimating the enzyme strength of duodenal contents be utilized for the diagnosis of pancreatic functional activity? It seems certain that it is reliable for ascertaining the patency or non-patency of the ducts of this gland. More experience with cases of disease of the pancreatic gland proper is necessary before it will be definitely known whether the method is applicable to the diagnosis of the functional activity of this organ. From the few cases offered in the series, it would seem that the method lends itself to prognosticating qualitative and quantitative variations in the strength of the pancreatic external secretion.

It is well known that very little idea of gastric function is pos-

sible from quantitative tests of the ferments elaborated by the human stomach, and yet this does not preclude the possibility of more reliable information of the pancreatic gland being obtained by this method of testing. It will remain to be demonstrated whether moderate pathological changes in the tissue of the gland will evidence itself by variations in the titer of the enzymes of the external secretion.

The study of a vast clinical material, with a uniform method of collecting and testing the duodenal contents in these cases, will be necessary to establish the further value of this method.

Since writing this article for publication, the author has noted the appearances in the literature of the experiences of Frank²⁰ with this same method. Frank succeeded in obtaining duodenal contents in 60 per cent. of the persons he attempted. The cases were chosen at random and suffered no pancreatic disease. The duodenal contents in all these instances showed active alkali-protease where tested for. The other ferments were not investigated. The inability of Frank to obtain the duodenal material desired in 40 per cent. of his essays is probably due to too short a time being allowed for the metallic capsule to enter the duodenum. This is obviated in my series of cases, by passing the pump in the evening and allowing the entire night to elapse before aspirating the desired material. Even then, more than one attempt is sometimes required before success is attained. The procedure is a mild one, and only exceptionally objectionable to the patient.

The sincerest thanks of the author are offered to the physicians and surgeons of the attending staff of Mount Sinai Hospital for the privileges of studying clinical material in their wards; to Dr. Samuel Bookman, for kind suggestions and hearty coöperation. and to the House Staff of the Hospital (more particularly Dr. Mahler) for general assistance throughout the course of this work,

A STUDY OF EMPYEMA, WITH SPECIAL REFERENCE TO THE FEASIBILITY AND IMPORTANCE OF DEPENDENT DRAINAGE.¹

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THE large number of operations which have been done in recent years has added much to our knowledge of the pathological changes

²⁰ Archiv f. Verdauungs-Krankheiten, 1912, xviii, 121.

¹ Read before the College of Physicians of Philadelphia, November 6, 1912.

which have taken place and the mechanical conditions which have arisen in connection with the various disease organs or tissues on account of which the operations have been performed. Our opportunities for the study of a pathological condition are much improved when during the operation it becomes necessary to remove the diseased organ or tissue, as in appendectomies, gastrectomies for ulcers or carcinoma, or in operations for the removal of other tumors. Even when nothing is removed a free exposure of the affected part is often obtained, so that practical observations can be made from sight and touch. Yet from the large number of operations which have been done for empyema we have learned little in this way. The opening made in the chest wall is too small for inspection of the diseased parts within, in the presence of the escaping pus, and the finger is too short for palpation. Our efforts, of necessity, have been confined chiefly to bacteriological examinations of the pus evacuated and to a study of the relation of the pus collection to the preceding infectious condition of the lung, as pneumonia or phthisis. Robinson² says that the bacteriology is of interest in prognosis, but of no significance as regards treatment. All cases should be recognized promptly and drained freely, reëxpansion of the lung being the main purpose from the start. Most surgeons will probably agree with these statements.

In a previous paper³ on empyema I employed an illustration of a formalin-hardened cadaver specimen, from the department of applied anatomy of the University of Pennsylvania, of an empyema from which the pus had not been evacuated during life. The possession of this specimen is the result of an accident, it having been selected for injection with formalin as one in which the normal relations and conditions of the abdominal and thoracic organs should be found, and I used it for the first time to illustrate how easily a large empyema could be overlooked on inspection. I have come to the conclusion that it was worthy of a more careful study and that it might yield valuable practical information concerning empyema in general. When making a study of conditions in the dead body we usually obtain our material from the dissecting or postmortem room. This kind of a specimen could hardly be obtained from either. It must be specially prepared, and one must know that the unopened empyema is in a body before he prepares it, unless, as in this case, he happens to find it by accident after he has injected the body with formalin. The number of empyemas that find their way into the postmortem room unrecognized and unopened is probably very small, and those that do are usually so mutilated before the empyema is recognized that the preparation of a formalin specimen of this kind would be impossible.

² Boston Med. and Surg. Jour., 1910, clxiii, 561.

³ Internat. Clinics, 1906, 165; iii, 150.

The first incision and manipulations necessary to expose the empyema would render the injection of the formalin ineffective, and would distort the relations of the soft structures to each other. In the dissecting room the conditions would be similar or worse

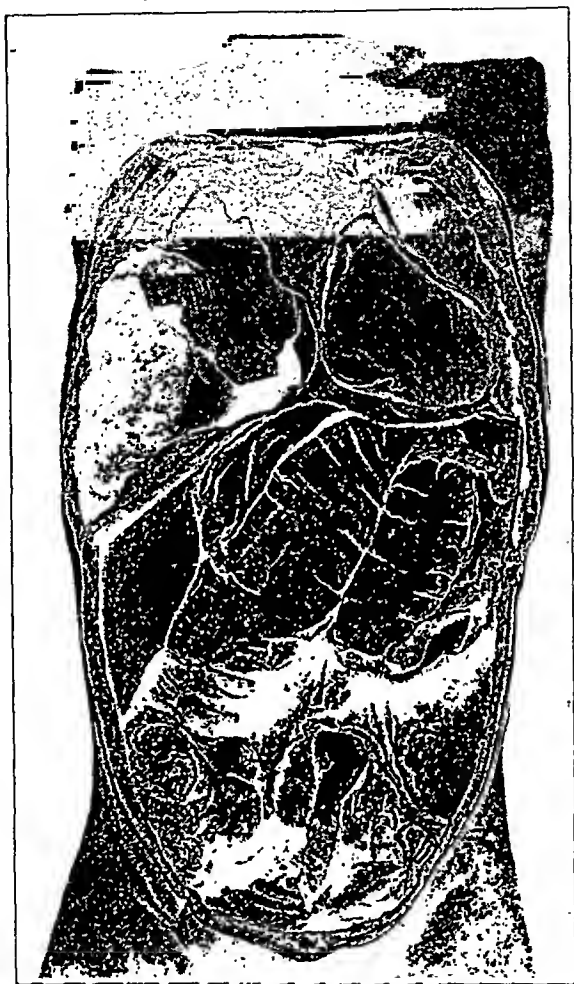


FIG. 1.—Formalin hardened cadaver specimen of an empyema which has been completely circumscribed by firm adhesions above between the lung and chest wall. A small portion of the lung, narrower than appears in the illustration, remained adherent to the diaphragm. The costophrenic sinus is much wider than normal from the pressure of the pus, while on the opposite side it is almost obliterated. The heart pushed to the left looks larger than it actually is because abnormally uncovered by the left lung which is crowded posteriorly and to the left. The placing of the drainage opening at the bottom of the normal pleural cavity (see Fig. 2) would have been easy and safe in this case, as it proved to be in the three cases in which it was so placed. The large intestine is much distended and the liver distorted and depressed by the pressure of the pus.

for the preservation of a similar specimen. If an opening had been made during life, such changes would have taken place that would have rendered the specimen less valuable, because we are most interested clinically in the empyema before the pus has been evacuated. Fig. 1 shows that there existed here the large common

and typical empyema, that giving marked and superficial dullness extending from the bottom of the pleural cavity a variable distance upward and merging below on the right side with the liver dullness. The displacement of the heart and liver are also typical.

A bacteriological examination of the pus debris remaining in the specimen was made by Dr. Rivas, of the University of Pennsylvania. He found in it leukocytes, lymphocytes, two kinds of bacilli, and a diplococcus. One of the bacilli was acid-fast, and suggested the tubercle bacillus. This was confirmed by a longitudinal section of the affected lung. The specimen had been lying in a strong formalin solution for about eight years, so that the pus debris from which Dr. Rivas made his examination had undergone such change as not to permit an exact bacteriological report. He concluded that the pus had been the result of a mixed infection. The most striking and important feature in connection with the specimen, in my opinion, is that the empyemic cavity, although a large one, is distinctly and firmly circumscribed below by the junction of the diaphragm and chest wall and above by adhesions between the lung and chest wall, so intimate and continuous that the line of cleavage between the two cannot be seen. I have seen a formalin preparation of a tuberculous empyema in which there were no adhesions between the two pleural layers, the lung lying completely collapsed against the spine. The probability is that in the latter there had developed a communication between a bronchus and the pleural cavity, resulting in a pneumothorax in the presence of a slight tendency toward adhesion formation. In my specimen there could be found no evidence of such a bronchial communication after a careful search of all surfaces presenting on the empyema, which was aided by a removal of a longitudinal section of the lung, about 3 inches wide, and extending the whole length of the lung. The firm and extensive adhesions sharply circumscribing the empyemic cavity were probably due to absence of a bronchial communication, and the fact that there was added to the tuberculous a pyogenic infection; the latter having a greater tendency toward adhesion formation than the former. This does not mean that tuberculous infection cannot produce the condition exhibited by this specimen. There is much vagueness in the literature concerning the existence of and the part played by adhesions in empyema. Many writers ignore their existence; some refer to bands of adhesions; while others seem to think their existence is largely a matter of chance. If they developed extensively in the presence of a mixed tuberculous and pyogenic infection, as in this case, I believe they are almost certain to occur in the acute pyogenic infections, including the pneumococcic, in which pneumothorax is rare. Indeed, the burden of proof should not be upon him who says that such adhesion formation is the rule, but upon him who says that it is not.

The empyema in this specimen extended from the bottom of the normal pleural cavity upward, anteriorly at one point as high as the second rib and posteriorly in a rather broad channel as high as the apex. It was one continuous cavity and no bands of adhesions crossed it. It was thoroughly walled off on all sides: above by close and firm adhesion between the lung and chest wall, and below by the union of the diaphragm and chest wall. I have based my study of empyema chiefly upon the character of the adhesion formation in this specimen, and upon the assumption that it is the rule in acute empyema. Many of the accepted teachings in connection with empyema, according to my judgment, have either taken no account of this feature or have not given it sufficient recognition. I have drawn some inferences from my study that I look upon more as suggestions than conclusions. The main definite conclusion I would draw is that dependent drainage in empyema, which calls for an opening as low as the eleventh rib or to the top of the twelfth rib in most cases, is not only feasible but comparatively easy and safe.

This massive type of empyema is frequently referred to as the unencysted or general, which implies that the pus is free to flow into all parts of the affected pleural cavity. The specimen strongly contradicts this conception, and shows, in my opinion, that practically all acute empyemas are encysted and localized by surrounding more or less firm adhesions, as in an appendicular or other abdominal abscess, or the small so-called localized empyema. The latter is localized, but probably no more so than the large one.

Morison⁴ says that the collecting effusion is first observed in the region of the fifth interspace, that is, diagonally farthest from the fixed point of the lung at its root, and that the reëxpanding lung last touches the chest wall in the same region. For this reason he makes this the point of election for the drainage opening. According to my experience most empyemas extend from the bottom of the pleural cavity, as in this specimen, a variable distance upward. I believe that the fluid begins to collect not about the fifth rib, but at the bottom of the normal cavity. Donaldson⁵ says that "the fluid products in pleurisy gravitate by their weight to the lowest portion of the cavity of the pleura and then gradually rise." The last part of the lung to reëxpand is probably that about the drainage opening, at whatever level it may be, where the external atmospheric pressure acts longest and to the best advantage. Considerations based upon this specimen suggest the following conception as to the conditions developing in and about an empyema. Most pneumonias affect the base of the lung, therefore the resulting pleural effusion should begin at the base of the pleural cavity. But let us suppose that the infection involves a higher

⁴ Trans. Med. Chir. Soc., Edinburgh, 1907 to 1908, vol. xxvii.

⁵ Pepper's System of Medicine, iii, 487.

portion of the lung and reaches the pleura on the corresponding portion of the external surface of the lung. If adhesions develop between the visceral and parietal pleurae, here, there can be no empyema, because there is no space in which the fluid can collect. If no adhesions develop the excess of fluid which results from the pleurisy falls immediately to the bottom of the pleural cavity and prevents adhesions between the surfaces over which it continues to fall. It should collect first in the costophrenic sinus, pushing the lung here away from the chest wall and diaphragm and the latter two from each other, as in the specimen. I would again agree with Robinson when he says that he is "not in sympathy with Fowler, who says that adhesions may occur in the costophrenic angle, raising the level of the bottom of the cavity so that the drainage need not be at the lowest point." Such adhesions might develop after a drainage opening had been made, but are not likely before. The accumulating fluid pushes the serous surfaces apart, but sooner or later where they are in contact above the pus collection and around the whole lung the approximated surfaces develop adhesions, weak at first but gradually growing firmer. In this way the pus becomes walled off all around by adhesions between the lung and chest wall, and probably some part of the diaphragm. This walling off is much more likely than with the average pus collection in the abdominal cavity, because in the pleural cavity the pus is less likely, from the nature of the cavity and the usual position of the patient, to move about. For the same reason a pelvic infection is less likely to give rise to a general peritonitis than one in the appendix or gall-bladder region. The cadaver specimen shows clearly that such a walling off occurred in this case, and that it usually occurs in empyema is strongly indicated by the fact that when a patient is changed from the sitting to the recumbent position there is little or no variation in the upper line of dulness. Movable dulness is probably rare in empyema, except perhaps in the early stages, before the adhesions have become strong enough to withstand the pressure of the pus under the influence of gravity. Donaldson says: "Once formed, these effusions (of pleurisy) are but slightly movable and but little displaced by the varying positions of the patients, unless the quantity be very great and no adhesions or bands have been made." He also says, "The serous transudations of hydrothorax always occupy the most dependent portion of the cavity." In other words, the fluid in the latter moves about under the influence of gravity. In an empyema the weight of the pus might cause a slight change in its position by pressure against the more or less soft lung. We know that the upper line of dulness in the sitting position is not straight but curved, the curve varying more or less, and that it does not change materially when the patient is placed in the recumbent position. The varying curve of this line is probably dependent

upon the position occupied by the patient during the development of the limiting adhesions. The absence of movable dulness as determined by percussion before and after a change in the position of the patient should be a sufficient guarantee that the pus has become circumscribed by adhesions in any given case.

The adhesions probably developed early and became stronger as the quantity of pus, and therefore its upward pressure increased, so that they held the adherent surfaces of the lung to the chest wall while the under surface of the lung removed from the chest wall was being pushed upward, the pus therefore reaching its highest level a variable distance from the chest wall. Above this level, especially when the pus collection is large, the percussion note is often hypertympanic—Skoda's resonance—particularly in the first and second interspaces anteriorly. In the formalin specimen the pus at one point reached as high as the second rib, so that in large collections the first and second ribs or interspaces anteriorly cover about all of the lung above the pus that comes as close to the skin surface. Posteriorly and above the first rib anteriorly it is covered by a much thicker layer of muscles and other tissues. The inference to be drawn is that the lung is more tympanic anteriorly in the first and second interspaces because it is nearest to the surface here. Skoda's resonance is explained by a retraction and relaxation of the lung from its elasticity and the upward pressure of the pus. This implies that the lung is being floated upward by the pus causing it to become relaxed. It has seemed to me that retracted and relaxed lung must be more or less functionless according to the degree of collapse, resulting from the relaxation. If its air cells are full of air and functioning it can hardly be collapsed. The support which the lung obtains from its firm attachment to the chest wall in its whole circumference must aid it in resisting the upward pressure of the pus and in keeping its air channels open for respiration. The lung is not floating in the ordinary sense on the fluid pus, and therefore largely collapsed and functionless, but is probably trying to maintain its function with the aid of the extensive firm adhesions, the atmospheric pressure exerted through the trachea, and with the aid of an increase in the capacity of the thorax produced by the auxiliary muscles of respiration. The portion of the lung tissue caught between this air pressure above and the pus pressure below is probably compressed and condensed, not relaxed. In the normal lung conditions the tidal air is only about one-third of the air contained in the lung. Necessity may now increase the proportion of the tidal air in the functioning portion of the lung, so that the hypertympany may be the result of overdistended, not relaxed lung. Auer and Meltzer⁶ say that the actual necessity of respiratory

⁶ Jour. Exper. Med., 1911, xiv, 569.

function for the mere maintenance of life amounts only to a small fraction of the normal respiration, and that the extent of the changes of gases occurring in normal respiration with a closed thoracic cavity exceeds greatly the need for the maintenance of life, since normal respiration is provided with an abundance of factors of safety. Necessity demands in an empyema that any still functioning portion of the lung shall work to its full capacity. It is generally agreed that the lung on the sound side is doing compensatory work, why not any sound lung on the affected side? That it probably does so is strongly indicated by the fact that a patient can live with a large empyema on each side, and the fact that he can live under these circumstances, indicates that the pressure of the large collection of pus on each lung is being largely offset by the extensive firm adhesions in the whole circumference of each lung. These began to develop early and resisted with increasing firmness the increasing pressure.

If a considerable portion of the lung is so functioning then it follows that this portion is occupying about its normal proportion of the thoracic cavity, and the portion which formerly occupied the space now represented by the empyemic cavity must be more or less compressed and condensed below the functioning portion. The adhesions were developed in the early stages between surfaces about in their normal relations to each other, and they probably continued to hold these surfaces together against the pressure developing later from the accumulating pus. This means, in my opinion, that the adhesions will not seriously hinder the reexpansion of the lung after the pus has been evacuated, and that the cavity is to be filled by reexpansion of that portion of the lung which presents upon or projects into the cavity. The adherent surface of the lung is about where it should be when the lung is fully expanded, and therefore the adhesions should not be broken up to favor reexpansion of the lung.

Elsberg⁷ reported some interesting facts concerning pneumothorax, observed in experimental work on dogs. Many of the dogs either died suddenly as soon as an opening was made into the pleural cavity, or a violent expiratory dyspnea ensued, soon followed by rupture of the mediastinal septum, double pneumothorax, and death. While most of the dogs stood well, a small opening in the chest wall, sudden heart stoppage or dyspnea, and death followed in some instances. The larger the opening, however, the more likely is the occurrence of serious interference with the respiration. In almost all the animals in which the size of the opening approached or exceeded that of the diameter of the trachea, when the dog was lying on its back, dyspnea and death followed. It made no difference in what part of the chest wall the opening was made. The

⁷ New York Med. Rec., 1908, lxxiii, 846.

cause of the rapid death seems to be the development of the double pneumothorax. If a dog will die of a total double pneumothorax a man should. But it is now known that a double empyema may be opened on both sides at the same operation and the patient live. Hellin,⁸ after a study of 113 cases collected from the literature and 1 of his own, makes some very interesting statements in this connection. He says: "The question of a double empyema is closely related to that of a double pneumothorax. *A priori*, one would expect that a simultaneous opening of both pleural cavities would prove fatal. At first it was considered best to open the second pleural cavity after the first had been closed. (An interval of one hundred and fifty days was allowed to elapse in one case.) But compelled because of the severity of the constitutional condition, it was gradually found that the interval between the opening of the two cavities could be shortened until both were opened at the same operation. The skeptic can convince himself that the classical theory born of a fear of a double pneumothorax is unfounded, since the patients do not cease to breathe in spite of the two opened pleural cavities." Hellin in his case found that the cyanosis occurring during anesthesia disappeared on the opening of the pleural cavities. In experiments on dogs he noted that some of the animals survived even after the collapse of both lungs if the opening in the first cavity was closed. Auer and Meltzer showed that while from the opening of the pleural cavity in the dog, collapse of the lungs, dyspnea, and death occur, if the opening were closed after the collapse of the lungs had occurred, the dog would continue to live. Only an open pneumothorax causes dyspnea. When the cavity was closed, even though the lungs have recently collapsed, an inspiration will cause some distention of the lungs and an inspiration of air into them. An expiration will cause a compression of the lungs and a removal of the carbon dioxide. Hellin⁹ inferred from his studies that a total double pneumothorax was not necessarily fatal, but that, as in caissons, it is chiefly in the suddenness of the change of pressure that the danger lies. But he assumed also that simultaneous opening on both sides of a double empyema gave rise to a total pneumothorax on both sides. Fabrikant¹⁰ asks if we may not hope that under these circumstances pleural adhesions will prevent collapse of both lungs. The formalin cadaver specimen gives an affirmative answer to this question. It is possible that the adhesions in the early stages may break down at some point and admit air to any open part of the pleural cavity above; but this would probably be very rare, if it occurred at all. The empyema specimen which represents probably the great majority of this massive type shows

⁸ Berlin. klin. Woch., 1905, xlii, 1415.

⁹ Archiv f. Klin., 1907, lxxxii, 866.

¹⁰ Deutsch. Zeitschr. f. Chir., 1911, cviii, 584.

clearly why a patient can live after the simultaneous opening of a double empyema on both sides. The air is admitted not into the whole pleural cavity of each side, but into only the strongly walled off pus cavities, which are now extrapleural in the sense that an appendiceal abscess becomes extraperitoneal. The atmospheric pressure can now exert its effect only upon the surface of the lung presenting on the empyema which is buttressed against a threatening collapse by the strong adhesions which before the opening was made protected it against the severe pus pressure. The atmospheric pressure is always the same, but the pus pressure will probably vary with the quantity of pus present, so that the immediate effect of the drainage opening on the lung will probably depend upon the difference in the two pressures one way or the other. It is my impression that I have seen patients breathe better after the operation when they are resting quietly in bed, and that I have seen cases in which the breathing was not as good.

The fear is sometimes expressed that the rapid evacuation of the pus following the usual opening made by the resection of a small portion of a rib will be accompanied by a dangerous change of pressure on the surrounding displaced organs, especially the heart. Hellin feared this and advised that all empyemas, unilateral as well as bilateral, be aspirated immediately before operation or one or two days before, in order that a too sudden change of pressure may not take place. I have seen a fairly large number of empyemas opened, but I have never seen such a danger threaten, and I believe that it is very rare. With each outflow of pus from the opening on expiration there immediately follows an inrush of air on inspiration to take the place of the pus evacuated, until when the pus is all evacuated its place has been taken by air at a pressure of about 15 pounds to the square inch. There is therefore probably no great change of pressure, and certainly not a sudden one. The ominous loud noise made by the air rushing in through the opening with each inspiration is in reality an indication not of danger, but of safety. As already stated, Hellin observed in his case of double empyema that the cyanosis occurring during narcosis, disappeared after the empyemas had been opened on both sides.

I have operated upon three and possibly four of the so-called localized or encysted empyemas. Since I believe that the usual large variety is in practically all cases circumscribed by adhesions, I believe that these names do not properly distinguish the small ones. The status of these cases has not yet been decided. I would suggest that they are practically all interlobar or between the diaphragm and under surface of the lung and that that is the reason for their small size, the pus becoming walled off by adhesions before it can get out of the fissure or the space between the diaphragm and under surface of the lung.

In connection with these small empyemas, Musser¹¹ emphasized the importance of firm and deep pressure in the intercostal spaces along the fissures and along the margins of the diaphragm or upper borders of the liver, to develop tenderness indicating the presence of small empyemas between the lobes of the lung or between the lung and diaphragm.

Murphy¹² says that many of the cases diagnosticated as abscesses of the lung are actually the result of empyemas communicating with a bronchus. Those diagnosticated as lung abscesses are very likely small and covered by more or less lung tissue, that is, they are interlobar. The pus breaks into the lung and ultimately finds its way into the air passages because it cannot well extend in any other direction. Depending upon the depth in the fissure at which it develops, the pus may or may not extend along the fissure and come to lie directly under the chest wall when a small area of absolute dulness could be detected. It may fail to do so because of its depth, when it will be covered by a layer of lung tissue, the dulness be relative, and air sounds be detected over it. The fissure is so oblique that it would be practically impossible to evacuate some deep collections by finding the fissure through an opening in the chest wall, and usually in such cases it is necessary to reach the pus by going through the lung tissue covering it, first shutting off the pleural cavity if necessary by suturing the lung to the chest wall in the circumference of the opening in the wall. The presence of sufficient adhesions here would render this unnecessary. When the pus collection is in the outer portion of the fissure directly under the chest wall the lung in the circumference of the empyema will be firmly adherent to the wall. In my 4 cases, I had 3 of the superficial variety and 1 of the deep. Small empyemas may develop between the base of the lung and the diaphragm, as already stated, but I have had no experience with this variety. It is said that these small empyemas frequently develop on the external surface of the lung between it and the chest wall. If they do it probably will be in an adherent portion enclosing a non-adherent area. The probability is, however, that such a condition is rare, and if a careful examination is made it is likely that in these cases the pus collection is close to some part of one of the main fissures. Robinson believes that most of these cases are peripheral abscesses of the lung. He refers to 2 cases which he saw at autopsy and 3 upon which he operated, in all of which the evidence as he interpreted it pointed to their having originated in abscesses of the lung. This evidence consisted in the fact that he found lung parenchyma devoid of pleura on the pulmonary side of the cavity. He expected to find the inner wall of the empyema made up of visceral pleura.

¹¹ Jour. Amer. Med. Assoc., January 5, 1907, xlviii, 24.

¹² Ibid., 1898, xxxi, 281.

I believe with Robinson that the pus will not often break through the pleura into the lung substance in the usual large empyema, that between the parietal and visceral pleuræ. As already stated, I believe that an interlobar empyema remains small because the pus becomes circumscribed soon from the fact that it cannot easily spread itself out in the fissure. Gravity probably has little effect on it, and the movement of the apposed pleural surfaces normally is probably slight. As soon as it becomes walled off, the pus can increase in quantity only at the expense of the lung which surrounds it. When it can no longer make room for itself by pushing the lung aside it will destroy it as it will destroy any other tissue which confines it, even bone. The pleura will probably first become necrotic and then the lung tissue and the process will continue until the pus finds an exit or kills the patient. Sometimes it will burrow externally through an interspace between the ribs. The lung is the weaker tissue, however, and therefore evacuation through the trachea, is the more common. We should not expect to find the pleura intact on the visceral side if the empyema has existed long enough to destroy it, and in many cases it probably has, by the time the empyema is opened, because this variety is usually the most difficult to detect.

The main purpose of any general study of empyema should be to improve our methods of treatment. In recent years we have had a number of valuable contributions looking toward this end. The main discussion seems to centre about the question of the method of drainage, and the consideration which has received most attention is that of the influence of the atmospheric pressure admitted through the drainage opening. Most cases get well sooner or later from drainage in the usual way, but in a considerable number the closure of the opening and cavity is much prolonged, or they may not close at all. Murphy¹² says that before the surgeon makes an opening into an empyema he should be reasonably certain that it will close later. He has discarded operation in all cases in which there is not an external opening or a communication with a bronchus. In other words, if air has not already gained entrance into the empyemic cavity through an external or an internal opening he will keep it out. He aspirates the pus and injects into the cavity a few drams or ounces of a 2 per cent. formaldehyde and glycerin solution, repeating the procedure at intervals of a few weeks as the effusion re-collects, until it has entirely disappeared. The fact that Murphy employs it in all cases, with the exceptions mentioned, attests its value and alone makes it a method which will be widely tested when it has been fully placed before the profession. As yet he has spoken of it only briefly in the discussion of papers by others. The formalin is said to render the cavity sterile and to favor the absorption of the

¹² Section on Surgery of the American Medical Association, 1909, p. 921.

exudate. Tennant¹⁴ tried the method, but in one case it failed him and a resection of a rib was done. It is the ideal method for combating the ill effects of atmospheric pressure on the external surface of the lung, and if it comes into general use there will be fewer cases calling for the severe Estlander or Schede operations. But it has not yet received general approval, and the prevailing treatment is that with drainage.

Many devices and methods of obtaining drainage with the exclusion of air from the cavity have been offered, and recently von Eberts¹⁵ and Robinson have added valuable contributions on this phase of the subject. Except for a brief attempt in one of my cases, which was soon discontinued, I have not as yet had any experience with these methods. It seems to me that before we can determine, with satisfaction, the relative value of suction or siphon methods of drainage we must first know approximately the limit of rapidity with which an empyemic cavity may be permitted to become obliterated. We are dealing with an abscess the walls of which are infected, and few surgeons will risk efforts at disinfection by irrigation. The rule is to permit the cleansing to be done by the natural processes after effective drainage has been instituted. In most cases in which drainage is employed in the usual way, without the use of suction, the cavity cleanses itself spontaneously and is obliterated by the expansion of the lung, sooner or later. Fraley¹⁶ reported a study of 500 cases of pleurisy treated at the Pennsylvania Hospital. About one-fifth of them were empyemas. No case was cured in less than four weeks. The average was ninety days, in which column were found one-third of the cases. All but 6 were cured in four months or less, and these were severely complicated. The shortest duration of convalescence obtained by Robinson with his method of rib trephining and suction drainage was four weeks, although in the one fatal case, in which death occurred two weeks after operation, the lung was fully expanded as shown at autopsy. We might argue with some force, therefore, that about four weeks are necessary, under the most favorable conditions, for the disinfection necessary before the cavity and drainage opening can close permanently. But the conditions vary. The degree of firmness with which the lung has become fixed in its compressed condition will affect the rapidity of expansion. The character of the infection will affect the rapidity of spontaneous cleansing, as will the presence of necrotic tissue in the wall of the empyema. According to Schädler, quoted by Hellin, the average duration of a unilateral empyema was fourteen and one-half weeks, in children nine weeks. Hellin says that the death rate in 1335 cases of unilateral empyema was 22.4 per cent.

¹⁴ Jour. Amer. Med. Assoc., August 15, 1908, p. 572.

¹⁵ Von Eberts and Hall, Montreal Med. Jour., June, 1910, 513; Annals of Surg., 1910, lii, 502; Ibid., 1911, liv, 59; Jour. Amer. Med. Assoc., 1912, lix, 264.

¹⁶ AMER. JOUR. MED. SCI., May, 1907.

or 299 deaths. The mortality in the double empyemas was 0.1 per cent. Robinson evidently made a careful study of other methods of suction drainage than his own, and of them he says: "It is well known to those who have performed rib resection and introduced tubes protected by rubber collars, rubber dam, adhesive plaster, lanolin, zinc ointment, gutta percha, cement, and other agents that leakage is of frequent occurrence and that at best it can only be prevented by the most painstaking and continuous efforts." In his discussion of this subject at the meeting of the American Medical Association in June, 1912,¹⁷ and at the meeting of the Pennsylvania State Medical Society, September 26, 1912, Robinson said that he now confines the use of suction drainage to only the most carefully selected cases.

It is an interesting fact that while the atmospheric pressure soon after the usual drainage opening is made is probably as great in the empyemic cavity as that exerted within the lung through the trachea, because the drainage opening is usually as large or larger in diameter than that of the trachea or larynx, in most cases the lung will expand later and obliterate the cavity. This is the more interesting when we take into consideration the fact that to the external pressure must be added the resistance of the normal elasticity of the lung and that of the inflammatory thickening of the inflamed pleura and adjacent lung tissue. In many cases this result will be accomplished in about four weeks without the employment of negative tension from suction drainage. Yet it is obvious that the lung can be expanded only by the atmospheric pressure coming through the trachea. The internal pressure in some way must gain on the external pressure. I have in several cases introduced my finger through the drainage opening at the time of the operation to find that I could not feel lung tissue or only a small portion of it. It was being held beyond the reach of the finger by the external atmospheric pressure exerted through the drainage opening. In 1 or 2 cases I have introduced the finger at intervals later to find that the surface of the lung could be felt to be approaching the opening. To my mind there is only one satisfactory explanation for it. The atmospheric pressure within the empyemic cavity must, in some way, be gradually diminished, so that the internal pressure can act to better advantage in expanding the lung. Otherwise the lung never could expand. In other words, the effect of the drainage opening usually employed is to provide more or less imperfectly, a negative tension within the empyemic cavity. We are all familiar with the sound made by the air which passes through the opening on inspiration during the after treatment even in the presence of a pus-soaked dressing. I observed in one of my cases that this sound ceased soon after the operation, perhaps in a few days, and in that case the cavity and sinus were closed in five weeks. I saw at the Philadelphia Hospital some years ago an

¹⁷ Jour. Amer. Med. Assoc., 1912, lix, 272.

empyema patient who had been operated on about two and a half years before. The drainage opening was more than an inch wide at that time. There was no sound in that case from the passage of air in or out, probably because the opening was so large. I could look through it into the cavity, and when I saw the case again a year later, as far as I could judge, no progress had been made toward the obliteration of the cavity and a cure. I have observed that the sinus is not long in closing after the sound made by the inrush of air on inspiration has ceased. Whether the sound ceases because the cavity has almost closed or the cavity closes more rapidly because the air has ceased to enter is uncertain, but it has seemed to me that if the entrance of air could be prevented the average case would be cured much sooner than it is. The small number of cases which I have had has prevented me from following up this idea as I would wish.

In my opinion the size and position of the opening have an important bearing upon the results of the operation. Elsberg showed that the size of the opening was an important factor in connection with the effects of experimental pneumothorax in dogs. If the opening made in most operations remained afterward as large as when made, I think that in many cases the lung never would expand, because it would be practically as large as that of the trachea or larynx, so that the external atmospheric pressure would remain constantly as great or greater than the internal pressure. It seems to me that the external opening must become smaller than the internal, or the tracheal diameter, before the lung can expand. After the usual operation the falling in of the soft tissues contracts the opening, which is further filled by the walls of the drainage-tube, and the lumen of the tube and the space around it are more or less choked up continually by the escaping discharge and fragments of fibrin. The air already in the empyemic cavity is becoming absorbed, and if a smaller quantity passes in than is being absorbed the external pressure on the lung is being diminished, so that the internal pressure coming through the trachea remaining the same the lung slowly expands. The excision of several ribs may be advisable to get nearer to the bottom of the cavity, but not to provide freer drainage. Through-and-through drainage by two openings with a tube in each and one higher than the other, in my opinion, is worse. The higher opening will always be admitting air freely, because the pus will be escaping entirely by the lower, so that the upper will be a strong factor in preventing reëxpansion of the lung. The term free drainage in connection with empyema has not the same meaning as with abscesses in other parts of the body. In many abscesses an incision is made from one end of the abscess to the other, and lays the cavity wide open. The Estlander operation for chronic empyema provides such an opening, and the result shows what is to be expected from it. The free admission of atmospheric pressure permanently prevents reëxpan-

sion of a large portion of the lung, which causes a marked sinking in of the side of the chest and a corresponding loss of lung function. The small opening usually employed in acute empyemas, if placed at the bottom of the cavity, would provide drainage quite free enough for the average case.

Robinson says that in the early stages, with the drainage opening at the bottom of the cavity, suction drainage will not be necessary. I am, particularly, trying to show that this will be true for most cases. In 2 cases I made the opening by resecting a small portion of the tenth and in 3 cases the eleventh rib near the spine. By dividing the intercostal tissues in the latter to the top of the twelfth rib practically the very bottom of the cavity was reached. I did this because of observations made on the formalin specimen, which shows that in that case at least there would have been no difficulty in making such an opening, and I found in my cases that it was about as easy and safe as resecting the sixth or seventh rib. A small puncture wound was made in about the seventh interspace or where the aspirating needle demonstrated pus. A somewhat rigid probe or a long grooved director, curved at the end, was then introduced through this opening and the end made to seek the lowest limit of the empyemic cavity, which usually corresponded to the bottom of the normal pleural cavity near the spine. The curve permitted the end of the instrument to be turned toward the surface where by careful palpation it could be felt by the finger outside over the corresponding interspace, usually the eleventh. A vertical incision was then made over this area, the eleventh rib exposed, and a small portion of it excised in the usual way. The probe or grooved director was then pushed outward through the pleura if it had not been already opened and a closed hemostatic forceps introduced at this point. The finger introduced through the opening thus made feels the twelfth rib below and the diaphragm at the bottom of the cavity. A drainage-tube is introduced after extending the opening by incision to the top of the rib below. A suture or two may be used to diminish the size of the opening slightly, but free drainage must be the first consideration. During the operation I have placed the patient in the prone position advised by Elsberg, and have found it satisfactory. In one case, as I was about to make the preliminary incision for the introduction of the probe, I happened to look at a clock and I concluded to time the operation. When the drainage-tube was in and the gauze dressing applied about four minutes, not more than five, had elapsed. With such an opening the empyema will be perfectly drained in almost any position the patient is likely to occupy. The shoulders will probably be higher at all times than the opening, the advantage increasing the more nearly the patient assumes the sitting position. The opening is at the bottom of the narrow space between the diaphragm and chest wall, so that all of the discharge will constantly gravitate toward it and will tend to prevent the entrance of air

in so far as it continues to fill the space in and around the tube. Usually I have not been greatly concerned about fragments of fibrin choking the tube, because I have felt that the drainage was free enough around the tube, and through it around any fibrin that became lodged in it. At any rate it will give no more trouble than with a higher opening. When we consider that we can in a short time evacuate the accumulation of weeks through the ordinary aspirating needle, it becomes evident that not much space is necessary with such a low opening for the continuous evacuation of the discharge as it forms. Nor have I been concerned about the falling in of the drainage-tube, since it is usually directed upward as well as inward, and would have to travel against gravity to get inside; and if it did so, would be kept by gravity at the opening so that it could easily be fished-out with a forceps

Agnew¹⁸ applied the principle of dependent drainage in old empyemas with persistent sinuses, but maintained through-and-through drainage with a tube passed from one opening to the other. Ashhurst¹⁹ employed the same method of drainage from the beginning, and says: "I have seen a number of cases in which this plan has been systematically carried out with complete success." It seems reasonable to assume that the lower opening drained all the pus in Ashhurst's cases, since pus could escape from the upper opening (the patient usually occupies the semirecumbent position from the beginning and soon the upright) only if the cavity were full of pus, when the plan would hardly have been regarded as a complete success. The important point demonstrated by Ashhurst, in my opinion, is that an intercostal dependent opening only large enough apparently to pass the drainage-tube gave satisfactory drainage. But we have many surgeons who employ such an opening usually in the sixth or seventh interspace, especially in children. If the drainage is satisfactory through such an opening it ought to be better with the opening in the eleventh interspace. Only a scarcity of cases has prevented me from trying the low intercostal opening.

Some surgeons make efforts to remove fragments of fibrin at the time of operation. I have felt some concern about them because they were in a pus cavity and were probably made up of necrotic material. I had one experience, however, that modified this opinion. On introducing my finger through the drainage opening I found the pleural surfaces, parietal and diaphragmatic, covered uniformly as far as the finger could reach with a soft layer of fibrin about an inch in thickness, which could easily be swept off with the finger. It seemed obvious that the whole surface of the cavity was so covered and that it was all infected material. As it could not be removed I watched the after course of the case with much interest. The sinus closed and the patient was discharged in

¹⁸ Agnew's Surgery, vol. i, pp. 344 and 345.

¹⁹ Principles and Practice of Surgery, 1893, sixth edition, p. 410.

about five weeks. The layer of fibrin gave no trouble. It did not escape through the drainage opening unless it liquefied, which is unlikely. It is more probable that it remained and became organized into a thickened pleura. I did not discover such a deposit on the pleural surface in any other case. It suggests that in the pleural cavity we have the serous, serofibrinous, and fibrinous varieties of inflammation, as in other serous cavities, and that the thickened pleuræ found in some old cases at operation may be due to the organization of such deposits. Thomson and Miles²⁰ say: "Even in comparatively recent cases the pleura is thickened and covered with masses of flaky lymph, which may be an inch thick. In some cases of long standing this fibrinous exudate becomes organized and the pleura is greatly thickened."

In those troublesome cases in which the affected lung fails to expand after a prolonged period the last resort is a thoracoplasty, by the Estlander or Schede method, with or without removal of the thickened pleura covering the exposed part of the lung. Since the latter will not expand to obliterate the cavity the ribs overlying it are removed, permitting the weakened chest wall to fall in against the lung. The operation is frequently a severe one and the resulting deformity marked. The lung remains permanently collapsed in large measure, which with the sinking in of the chest wall produces a condition which is far from desirable. Robinson believes that these operations are too often employed in cases which are by no means beyond the possibility of reëxpansion. I believe that this is true. Ochsner²¹ has made an important contribution to the treatment of these cases. In 14 cases he injected the cavity with Beek's bismuth paste, and all but 2, which were still under treatment, were cured. He has used it only in cases with sinuses, although, he says, it has been suggested to aspirate the pus in the empyema and to inject the paste into the cavity through the cannula. While the method appears to be decidedly better than thoracoplasty, it would hardly be advisable to employ it to the exclusion of the usual drainage method, which results in a cure in most cases, with almost if not complete reëxpansion of the lung. Any paste retained permanently must be at the expense of the non-expansion of a corresponding portion of the lung. The cases calling for the Ochsner method, or thoracoplasty, are usually chronic not in the sense that they have long existed without being opened, but are cases which were opened in the acute or subacute stages and became chronic while waiting for the lung to expand. It is likely that in the chronic cases the lung has expanded considerably since drainage was begun, and therefore will require a much smaller quantity of the paste than if injected at the time the pus was first evacuated.

(To be continued.)

²⁰ Manual of Surgery, fourth edition, ii, 318.

²¹ Annals of Surgery, 1909, 1, 151.

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by Hobart A. Hare, M.D., Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor of Therapeutics in the Jefferson Medical College of Philadelphia. Vol. iv, December, 1912, pp. 381; 62 illustrations. Philadelphia and New York: Lea & Febiger.

IN the final number of *Progressive Medicine* for 1912, Edward H. Goodman contributes, for the first time, the article on diseases of the digestive tract and allied organs. Readers of *Progressive Medicine* will recall that for the past few years this section has been written by R. S. Lavenson, whose carefully prepared and interesting articles will long be remembered as models of this type of critical medical literature. The selection of Goodman as Lavenson's successor will meet with general approval, not only because of his well-known work along the lines of gastro-intestinal diseases and physiological chemistry, but also because of his present admirable contribution, which makes it evident that the high standard set by his able predecessor is destined to be maintained.

Goodman covers thoroughly the more recent and interesting problems in relation to diseases of the gastro-intestinal tract. Among the subjects which he discusses is the analysis of gastric contents, the pathological physiology of the stomach, gastric ulcer, and carcinoma. Under the intestine some of the newer subjects touched on are the intestinal flora, chronic intestinal stasis with special reference to the work of Lane, and cecum mobile. After devoting a few pages to the liver, he discusses at more length chronic pancreatitis, functional tests of pancreatic insufficiency, and a number of other interesting pancreatic conditions. His entire article occupies 124 pages.

Under diseases of the kidneys, John R. Bradford, takes up particularly hemaglobinuria, the functional activity of the kidneys, movable kidney, albuminuria, and cystic disease of the kidney.

The subject of genito-urinary disease is well handled by Charles W. Bonney. After discussing affections of the kidneys, ureter and bladder, he turns his attention to the prostate, urethra, and numerous miscellaneous conditions.

In a contribution of 108 pages, Joseph C. Bloodgood writes most instructively on shock, anesthesia, infections, tumors, and the surgery of the skin, muscles, fasciæ, tendons, and bones and joints. Although it is impossible to mention in detail the many subjects he considers, attention should be drawn particularly to his discussion of preventive surgery, anesthesia and blood pressure, epithelial tumors, benign connective-tissue tumors, myositis, and the operative treatment of bunions.

The concluding section of 80 pages on practical therapeutics by H. R. M. Landis, deals not only with a number of the newer remedies, but also covers such subjects as antidiphtheretic serum, vaccines, climate, and heliotherapy.

The entire volume is of unusual interest and forms a valuable addition to the preceding volumes published during the past year
G. M. P.

PSYCHOTHERAPY. By JAMES WALSH, M.D., Ph.D., Dean and Professor of Functional Nervous Diseases and of the History of Medicine at Fordham University School of Medicine, and of Physiological Psychology at the Cathedral College, New York. Pp. 806. 34 illustrations. New York and London: D. Appleton & Co., 1912.

It would have been impossible for Dr. Walsh, who is equally well known for his extra medical knowledge, to have produced anything else but an interesting and philosophical work. It is, of course, very well written, and, as would be expected, full of historical references. The most interesting part of the book, to the reviewer at least, is the part upon the history of psychotherapeutics.

The plan of the work is to take up the general question of psychotherapy in the history of medicine, in which everything that has a bearing is discussed, such as signatures, pseudoscience, mental healing, nostrums, talismans, charms, and faith cures. In the next section, on general considerations, the influence of the mind on the body, body on the mind, secondary personality and hypnotism are taken up. In the third the individual patient is discussed and his general work, pleasures, and in fact his whole day is critically analyzed and suggestions given. Then comes the chapter on general psychotherapeutics, in which the principles are laid down, this being followed by a section on general adjuvants and treatment, such as exercises, suggestion, aversion of mind, habit, and then follows special psychotherapy which takes up almost every disease under the sun. It is, as the author states, the only complete book on psychotherapy.

It would be impossible to review a work of this kind in full

because to do so it would be necessary to write a smaller one. Suffice it to say that it is such a work as should be in the hands of the patient as much as in the hands of the physician, for it is optimism that Dr. Walsh preaches. "Nothing is as bad as it seems, and if you only make up your mind to it and cheer up, everything will be better." For example, if the general practitioner who buys this book wants to look up even such a hopeless disease as hemiplegia, he is met with the statement that Pasteur had a stroke at the age of fifty and yet lived for twenty years, and did his best work after it. What could be more cheerful and promising? Specifically, Dr. Walsh's advice is excellent. He believes in common sense methods and takes advantage of any legitimate means that he can in treatment. He believes in the judicious use of hypnotism. One fault of the work, if there is a fault, is the fact that there is a great deal of repetition, but this no doubt is the purpose of the author, for he perhaps means that if anyone wants to look up what should be done under a certain disease he will find complete advice. Necessarily if every disease is discussed in the same manner repetitions must occur. Were it not for this, such a book could be written in about 200 pages instead of 800.

The average neurologist, however, who will expect to find a discussion of psycho-analysis, as taught by Freud, will be met with disappointment, for Freud is dismissed in a trifle over a page. Dr. Walsh evidently believes that Freudism is only a fad, and classes it with osteopathy and Eddyism. Like osteopathy and Christian Science, however, it will remain and grow stronger. It is to be regretted that such an important subject should be dismissed so lightly and with such evident scorn. The reviewer is by no means an ardent Freudian. He believes, however, in common with those neurologists who have paid attention to it, that there is a great deal in psycho-analysis, and that it is by no means a fad and that it will live. It has been the style since Freud's work to condemn those who have either taken up or who favor it, rather than to discuss psycho-analysis on its merits, and the criticisms have been somewhat caustic and by no means always tinged with wisdom. The basis of the whole criticism is that Freud believes that most neuroses have as a cause some previous experience which in the majority of cases is sexual. Its critics always state that it is abhorrent to them to discuss sexual matters with the patient, and it does no good. As a matter of fact, the trained psycho-analyst does not discuss sexual matters with his patient because he wants to. He does it because he finds that he has to, and that the average normal person as well as the nervous patient has a great many ideas about sexual matters which need straightening out, and very often the basis of such a neuroses may be a previous sexual experience or sexual thought which the patient

many not be at all aware of. The truth of the matter is that the average doctor, in common with other humans, wants to get the most results with the least amount of effort, and that he very rarely desires to face the situation, especially if it is disagreeable. In our education sexual matters are always placed in the background, for it is a crime to discuss those things which are always before us, and it seems that it is a greater crime for the doctor to discuss them than for anyone else, and yet the doctor is supposed to heal! How long will we have to wait until, like Tanner in Shaw's *Man and Superman*, we will state facts as facts and truths as truths, and live accordingly?

T. H. W.

BLUTKRANKHEITEN UND BLUTDIAGNOSTIK. LEHRBUCH DER MORPHOLOGISCHEN HÄMATOLOGIE. Von Dr. med. OTTO NÄGELI, Privatdozent an der Universität Zürich. Second edition. Leipzig: Veit & Co., 1912.

THE second edition of Nägeli's "Blutkrankheiten und Blutdiagnostik" will be welcomed by all who are interested in the study of hematology. It has been very largely rewritten and much enlarged, and many new colored plates have been added.

Those familiar with the first edition of this work will find that the author still adheres largely to the teachings of the Ehrlich school. That he is not a passive follower is well known; many of his personal observations appear here for the first time. However, the reader is not presented with the facts to support one view alone, but a fairly impartial presentation is made, and from these the author draws his conclusions. In matters of controversy, the opposing interpretations of morphological or tinctorial abnormalities are stated.

Technical procedures are well discussed. Practically all of the stains which are useful in the study of the blood are given; the methods of staining are described, together with the best fixatives for a given stain. This applies to the staining of blood films and of sections of tissue as well. To the laboratory worker, one drawback is evident; the method of preparing the stain is seldom stated. Instead, one is advised to buy the prepared staining mixtures, usually from Grubler.

In the new edition the viscosity of the blood is fully considered. The inclusion of many observations by the author adds greatly to the value of the discussion.

The section on the red blood corpuscles, like other parts of the book, has been brought fully up to date. The pathological alterations of the red cells are taken up in detail, and there is an adequate description of each, well illustrated in the colored plates. As

examples, ring bodies, Howell-Jolly bodies, and chromatin dots may be cited. Normal and pathological regeneration of the erythrocytes is described in the embryo, in the normal adult, in anemias, in the embryos of animals, and in experimental anemias.

The discussion of the leukocytes is equally complete and illuminating. The various types of leukocytosis are considered in detail.

The blood findings in disease are well presented. This is true not only of the diseases affecting the blood-forming organs primarily, such as chlorosis, pernicious anemia, the leukemias, but also of all diseases in which changes in erythrocytes, leukocytes, or platelets are usually met. Fewer additions are to be found in this part of the volume, though here, as elsewhere throughout the treatise, personal observations of the author are in evidence.

It is a pleasure to record the fact that the author, unlike most of his German-speaking colleagues, has not been content to ignore the foreign literature. His pages teem with references to French, Italian, English, and American authors. In fact, his thorough mastery of the literature of his subject explains the high value of the work the author has produced. Excellent bibliographies are appended to each chapter.

In a review it is impossible to give an adequate idea of the scope of a volume. Suffice it to say that the title of the present work expresses very clearly its contents. If any important morphological studies of the blood have escaped the notice of the author, the reviewer has failed to detect the fact. That he has placed insufficient stress on certain contributions is inevitable. The observations of Wright and his co-workers upon the origin of blood-platelets is a case in point, in the opinion of the reviewer.

Naegeli's "Blutkrankheiten und Blutdiagnostik" is unhesitatingly recommended as a valuable aid to the study of hematology.

R. S. M.

A CROSS-SECTION ANATOMY. By ALBERT C. EYCLESHYMER, B.S., Ph.D., M.D., Professor of Anatomy, St. Louis University, and DANIEL M. SCHOEMAKER, B.S., M.D., Associate Professor of Anatomy, St. Louis University. New York and London: D. Appleton & Company, 1911.

IN recalling the advances in gross human anatomy during the last twenty-five years, the introduction and wide use of two methods of study—hardening *in situ* and cutting frozen sections—stand out conspicuously as most productive factors. The publication by Professor His, in 1878, of his studies on bodies hardened by injections of chromic acid solutions, and, later, the dissemination of his findings by means of models cast from his preparations,

wrought a revolution in visceral anatomy and exposed many current errors regarding the form and relations of important organs. Scarcely less important, although not so generally appreciated, was the appearance, in 1872, of Braune's splendid work, "*Topographisch-Anatomischer Atlas. Nach Durchschnitten an gefrorenen Cadavern.*" Although by no means the pioneer in this important field of anatomical observation—for, among others, Pirogoff had produced his monumental work twenty years before—Braune did more than any of his predecessors to awaken an interest in sectional anatomy and to make available the results of such study.

The introduction of formalin as a preserving and hardening fluid marks a new era in anatomical technique, especially in connection with frozen sections. This combination, first used by Gerota in 1895, is now so highly valued and widely employed by anatomists the world over, that it is justly regarded as indispensable. Thanks to these improvements in anatomical methods, our present understanding of the form and relations of the various parts of the body, especially the viscera, is far more accurate and complete than when dependence was so largely placed on dissociation. Moreover, the advantages of combining the older and newer procedures, that is dissecting the sections of the formalin hardened bodies, are so pronounced for certain lines of work, that the method is now often followed, yielding preparations in which the parts may be separated or assembled, like the pieces of a picture puzzle.

Appreciating the necessity of cross-sections as a means of acquiring accurate notions concerning topographical relations, Dr. Eycleshymer and his associates, Drs. Schoemaker and Smith, have undertaken to make such important data available, when access to frozen sections stored in anatomical institutes is impracticable. Indeed, in no other field of anatomy do careful drawings offer so satisfactory a substitute for actual preparations as in the one under discussion. How adequately these gentlemen have fulfilled their self-appointed task, is shown by the admirable atlas before us.

The work consists of four divisions: (1) Introduction, giving an interesting historical sketch of the development of sectional anatomy and a description of the material and methods used in the preparation of the plates; (2) illustrations of the cross-sections, with explanatory text and key-figures; (3) topography of the organs, including a critical review of the position of the most important, and (4) bibliography.

The atlas comprises 102 quarto plates, of which 87 picture the upper surfaces of 113 consecutive cross-sections, supplemented by 14 key-figures and one plate illustrating the vertebral levels of the thoracic and abdominal viscera. Of the 113 cross-sections, 19 are of the head and neck, 29 of the trunk (including a series of five sections through the pelvis of a female subject), while the remaining ones are of the extremities, the upper limb contributing 26 and the lower 39 sections.

Recognizing the importance of thorough orientation for an adequate understanding and appreciation of cross-sections, the authors have wisely taken special pains to supply the necessary correlation by a generous series of admirable key-figures. The care with which these have been prepared is one of the features of the work calling for particular commendation. Thus, not only is the surface level of any given head-section seen by a glance at Key-figure 1, but reference to the following two figures shows in detail the relations of the section to the superficial and deeper structures, the third figure being a mesial sagittal section of the head, on which are indicated the planes of all the sections. Moreover, these key-figures are not merely arbitrary sketches, on which the approximate levels of the sections have been drawn, but are based on reconstructions from the sections themselves and, consequently, insure accurate correspondence between the details of the sections and those of the keys.

The sections throughout the work are on a uniform scale of four-fifths natural size, thus affording ample space and size for even small details without resorting to plates of inconveniently large dimensions. Accuracy in the illustrations was secured by tracing the surface of each section directly on a sheet of thin glass, subsequently transferring the outlines to paper by retracing under transmitted light. The technical excellence of the finished drawings, as reproduced in the printed plate, is most gratifying, for these are not only clear and exact, but represent the textures of the cut structures with so much fidelity and artistic feeling, that one recognizes a likeness, not merely a diagram.

The difficult problem of labelling the many structures to be seen in the sections has been solved very satisfactorily. The necessary leaders, in some cases fourscore or more in number, are definite and distinct, being carried, with judgment and taste, beyond the margins of the sections. At the end of each leader, the name of the indicated structure, printed in neat legible type, supplies the means of ready identification. In addition, each leader is consecutively numbered, so that the index and text references may be conveniently located. The nomenclature of the plates is uniformly the B.N.A., but, where necessary, the synonyms in the older terms are given in the descriptive text.

The value of the plates illustrating the head-sections passing through the brain has been materially increased by avoiding the uninteresting repetition of the details of the two sides. This advantage has been gained by doubling the number of actual sections on one side of the head, so that while the upper surface of the section of the usual thickness is shown on one-half of the plate, the other half is devoted to the upper surface of the intervening section. In this way, the views of the sectioned brain have been doubled, without adding to the number of the plates. By skilful

use of shadows, the relations of the levels of the two surfaces are made evident.

It is, perhaps, in the study of the cross-sections of the trunk, that the value of the reconstructed key-figures will be most appreciated. These key-figures comprise a series of four plates, representing the body from the shoulders to just below the trochanters. Although only approximately two-fifths natural size, and, therefore, about one-half the scale of the sections, they are sufficiently large to supply satisfactory orientation. The first depicts the skeleton in relation to the surface contour, and shows the planes of the 26 sections and their vertebral levels. The second key-figure, done in colors, exhibits the relations of the cross-sections to the muscles of the antero-lateral body wall, the skeleton being shown in outline. The third key-figure, also in colors, gives the relations of the planes of the sections to the heart and great vascular trunks, and to the brachial, lumbar, and sacral plexuses. The fourth key-figure, made entirely by reconstruction, represents the thoracic and abdominal viscera and displays their mutual relations, as well as their relations to the levels of the sections and to the skeleton.

In order to insure an understanding of the five cross-sections of the female pelvis, by Dr. Carroll Smith, which supplement the trunk series of the male body, a key-figure, representing a mesial sagittal section of the pelvis, is provided. This figure was obtained by assembling the actual cross-sections and cutting them sagittally, in this manner securing accurate correspondence between the details of the sections and those of the key. In consequence of a full bladder and distended rectum, the uterus is somewhat elevated.

The cross-sections of the extremities also are elucidated by excellent key-figures, based on reconstructions from the sections themselves. The two key-figures of the upper limb, from the lower border of the insertion of the pectoralis major to the hand, and about two-fifths natural size, exhibit the relations of the sections to the surface, skeleton, muscles, bloodvessels, and nerves, and serve to recall the form and disposition of the structures usually studied in dissections. The same assistance is provided for the lower limb by two reconstruction keys of the thigh and leg and by two additional ones of the ankle and foot.

The division of the work relating to the topography of the thorax and abdomen is contributed by Dr. Peter Potter and embodies the results of his arduous reconstructions of ten adult bodies of male negroes. The measurements, as to vertebral levels, were taken from sections of formalin hardened bodies and recorded in a comprehensive table. The average levels, deduced from these observations, were utilized to construct the interesting and useful plate, in which the thoracic and abdominal organs are shown, from in front and in colors, projected in accordance with their average relations to the spine.

The bibliography assembles the titles of almost one hundred publications bearing upon sectional anatomy. The wealth of anatomical details contained in the atlas is made available by an excellent index, by means of which the exact location in the plates of any structure may be readily found. The index also serves to correlate the new and old terminology, by giving both names where confusing differences exist.

An accurate knowledge of the topographical relations of many parts of the body is, manifestly, so important, that not only the serious student of human anatomy, but also, and perhaps even more, the clinician should heartily welcome this important addition to his means of acquiring such information. As a piece of book-making, the work is admirable and a conspicuous example of the results obtainable by coöperation of authors, artist, and publishers. All of these are to be congratulated; moreover, this congratulation may be extended to American Anatomy, on the production from its ranks of a contribution of such high merit. G. A. P.

SALVARSAN IN SYPHILIS AND ALLIED DISEASES. By J. E. R. MCDENAGH, F.R.C.S., Surgeon to Out-patients, London Lock Hospitals. Supplement to System of Syphilis. By POWER and MURPHY. 150 pages, 11 illustrations and 3 plates. London, Oxford University Press, 1912.

THIS work fills an important place in the literature of syphilis of today as it describes in detail all that is known of salvarsan to date. The author describes salvarsan physically and to some extent chemically, explains its injection, estimates its potency, and impartially states its limitations, and demonstrates its advantages by reporting actual cases in point.

He enumerates the toxic symptoms sometimes experienced and believes that generally they are due to faulty technique in the administration and to failure to properly diagnose contraindications for its use in the patient; which, however, he claims are very few in number.

Fatal cases are ascribed to faulty technique and to the failure to lay the blame where it belongs, as a rule, namely in the disease. Contraindications are disposed of in four pages as being composed of serious visceral diseases.

In discussing the methods of administration the author gives precedence to the intravenous and advises repeated doses, given in pure *freshly* distilled water at body temperature.

The question of the Wassermann reaction and how it is influenced by salvarsan, is discussed in detail and examples are given

showing the reaction between the two under various conditions of medication and stages of the disease.

The treatment is applied in syphilis in all its stages and severities and conclusions drawn from actual reported cases treated by the author. The conclusions, based on facts and not theories, are as follows: (1) Salvarsan kills the spirochetes in the chancre, mucous patch, and condylomas. (2) in the secondary stage, repeated injections of salvarsan will give a negative Wassermann; (3) in the tertiary stage a negative Wassermann is obtainable and lesions clear up. But a negative Wassermann is not always to be desired here.

The drug is also useful in some of the other diseases due to protozoa and conditions like scurvy, malaria, psoriasis, etc.

If patients with lesions of vital organs or non-syphilitic nervous lesions are excluded; if only half doses be given in syphilitic nervous disease, and if patients be examined thoroughly beforehand, no fear need be entertained about using salvarsan, provided, the water used is freshly distilled the second time. E. L. E.

THE MECHANISTIC CONCEPTION OF LIFE: BIOLOGICAL ESSAYS.

BY JACQUES LOEB, M.D., Ph.D., Sc.D., Member of the Rockefeller Institute for Medical Research. Pp. 232; illustrated. Chicago: The University of Chicago Press, 1912.

A SERIES of ten essays, which as the title of the book indicates, have as their general tendency an attempt to analyze life from a purely physicochemical viewpoint. The subjects presented are the significance of tropisms for psychology, comparative physiology of the central nervous system, pattern adaptation of fishes and the mechanism of vision, physiologic morphology, process of fertilization, artificial parthenogenesis, prevention of the death of the egg through the act of fertilization, role of salts in the preservation of life, and the influence of environment. It is impossible for the reviewer, because of lack of training in this phase of biology, and therefore of lack of power of interpretation, to present the general biologic argument of these essays. One or two conclusions may, however, be summarized for the benefit of a medical audience.

In the opinion of Dr. Loeb, if life phenomena can be explained in physicochemical terms, "our social and ethical life will have to be put on a scientific basis, and our rules of conduct must be brought into harmony with the results of scientific biology." This it may be remembered is the argument presented by the late Christian A. Herter in his "Biological Aspects of Human Problems."

The chapter on "The Significance of Tropisms for Psychology"

closes with the suggestion that "under the influence of certain ideas, chemical changes, for example, internal secretions within the body, are produced which increase the sensitiveness to certain stimuli to such an unusual degree that such people become slaves to certain stimuli just as the copepods become slaves to the light when carbon dioxide is added to the water." Pawlow's work on the stimulation of saliva in the dog by acoustic and optic signals is quoted (Cannon's work on the influence of the emotions on the secretion of adrenalin is in accord with this), and leads the author to the observation that "it no longer seems strange to us that what the philosopher terms an 'idea' is a process which can cause chemical changes in the body."

The treatment of the various subjects presented is avowedly popular, and although the experimental material consists of the lower forms of life, the facts brought out and their discussion will prove of great interest to those interested in the underlying biologic aspects of medicine.

R. M. P.

ACROMEGALY: A PERSONAL EXPERIENCE. By LEONARD PORTAL MARCK, M.D., late President of the West London Medico-Chirurgical Society and Pathological Draughtsman to St. Bartholomew's Hospital. Pp. 60; 9 plates. London: Baillière, Tindal & Cox, 1912.

THIS book being the personal record of a man afflicted with acromegaly, possesses additional value, inasmuch as the subject is a physician who has recorded very minutely and most accurately his state. Although acromegaly may be present many years before a patient consults a physician for relief from some troublesome symptom, the gross change in appearance apparently having escaped attention, it is most strange that the author, a physician, did not perceive the change in himself, for he writes: "For some fifteen or twenty years, each day when I looked into the glass to brush my hair or to shave, there was a typical acromegalic literally staring me in the face; yet I never recognized the fact." And he adds: "One might say it was a case of a *secret de Polichinelle*. Many of my friends, medical and non-medical, knew that I was suffering from this peculiar and rare malady; they spoke about it among themselves; some of them even thought I knew it; but none of them broached the subject to me. The strange thing was that in my case the only one not in the secret was poor *Polichinelle* himself, with his heavy jowl, his pot belly, his big hands and feet. It is a remarkable example of how what is obvious may be overlooked."

Poor *Polichinelle*, indeed, but brave. Acts of heroism, deeds

of courage, sending the blood tingling through the arteries of every man are done daily and receive their mete of acclamation. They are done in the open, before an admiring crowd, in the presence of witnesses, on the impulse of the moment, before caution with her unobtrusive voice has time to be heard. Cheers of approval and the flashing of the news across the country are hand in hand with the deed of nerve and reward it. But do these public acts of heroism constitute all bravery? The physician who suffers with an incurable disease which must not be disclosed on account of the effect on his patients, who modulates the discord of a grown seeking his lips into the harmony of a laugh which hides the clang of joylessness, who struggles on day by day against increasing weakness, pain, and distress of mind and body, dedicating himself to the good of those to whom he swore allegiance when he became their servant, with ever the knowledge gleaned from experience mocking him with its malignant certainty that his illness must have a fatal termination in about such and such a time. Is this man any less a hero than he who performs the sensational but no whit braver act? The reviewer is reminded of the condemned murderer in the "Ballad of Reading Gaol:"

"But I never saw a man who looked
So wistfully at the day
I never saw a man who looked
With such a wistful eye
Upon that little tent of blue
Which prisoners call the sky."

Dr. Mark has achieved a really great thing in thus recording amidst the tortures of what he calls the "acromegalic state" his subjective and objective symptoms. With an impersonal viewpoint which is at times uncanny in the close analysis of his case he pens well and fluently his tragic state. There is no appeal to commiseration. There is no call for sympathy. He describes in cold language cold facts, as a physician might report a "case" but we, who read between the lines,

"With sad unhelpful tears and with dimmed eyes
Look after him and cannot do him good."

E. H. G.

PELLAGRA. By STEWART R. ROBERTS, S.M., M.D., Associate Professor of the Principles and Practice of Medicine, Atlanta College of Physicians and Surgeons, Atlanta, Ga. Pp. 272; 89 illustrations. St. Louis: C. V. Mosby Company, 1912.

IN this able treatise, Roberts has assembled the data which have accumulated thus far concerning pellagra, and given them a searching and discriminating consideration. His work comprises

an interesting study of the disease in this country particularly in comparison with its manifestations in Southern Europe and Egypt. As the author states, the book is not "devoted to upholding any special theory of etiology." The arrangement of material is orderly, and the style often impressive. Of particular interest are the chapters dealing with the general characteristics of pellagra, its geographical distribution, the history of its progress in Spain, Italy, France, Egypt, and America. Most significant, naturally, is the last chapter treating of the cause of this disease. Here are arraigned against each other in complete fashion the evidence for the corn theory, and for the infective theory. Roberts, while not championing either side, presents so many more arguments for the latter than for the former that the weight of evidence appears to favor Sambon, who considers the simulum fly as the carrier of a causative organism. The discussion, however, is impartial. As the author remarks, "The advocates of corn have had a hundred years and have not made out their case. Sambon's theory is but two years old, and is being investigated."

The recognition of the various manifestations of pellagra has been described with minute care, sometimes almost at the risk of repetition, with the end result, however, that the reader obtains a clear concept of the acute attacks, the subchronic, and chronic forms, and the periods of intermission. The pathological findings in the alimentary tract, skin, and nervous system are reviewed at length, as are also the abnormal features in the other systems of the body. Some emphasis is laid on the occurrence of lymphocytosis and an increased cell count (average 35) in the cerebrospinal fluid. Treatment is satisfactorily considered. There are abundant illustrations throughout, for the most part very illuminating to the text. These include a number of maps and diagrams showing the distribution of the disease and some admirable photographs of pathological sections from the nervous system. Roberts' work is one of the few that have appeared in English on this important topic, and should command the attention of students and practitioners. One assumes that it is a printer's error which causes on page 44 the astonishing information that "*maladie des saintes mains*," signifying in English, "the sickness of the main saints."

H. G. S.

A TEXT-BOOK OF GYNECOLOGY. By WILLIAM SISSON GARDNER, M.D., Professor of Gynecology, College of Physicians and Surgeons, Baltimore. Pp. 271; 138 illustrations. New York and London: D. Appleton & Co., 1912.

THIS book has been prepared to meet the demands of the medical student. With this aim in view, the author has confined himself

strictly to the fundamentals of gynecology; facts are stated as such without modification and with only sufficient elaboration to insure a thorough understanding of the subject. While the rarer diseases are passed by with only a few words, those which the student should master are clearly detailed from the standpoints of pathology, symptomatology, diagnosis, and treatment; the anatomy of each organ likewise receives its due share of description. With the exception of three short chapters on technique and post-operative complications, the arrangement and presentation of the text closely follows that of similar text-books; in no way has the author shown originality in presenting his subject so as to more deeply impress his ideas upon the student's mind. The illustrations consist of schematic sketches, photomicrographs, and photographs of gross specimens; herein lies the weak part of the book, for in many instances the pictures convey no idea whatever of the actual condition, and even the best of the illustrations might be vastly improved upon. With this exception the book deserves commendation; it briefly but clearly summarizes the principles of gynecology.

F. E. K.

RETINOSCOPY (OR SHADOW TEST) IN THE DETERMINATION OF REFRACTION AT ONE METER DISTANCE, WITH THE PLANE MIRROR. By JAMES THORINGTON, A.M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmic Surgeon to the Presbyterian Hospital, etc. Sixth edition; pp. 71; 61 illustrations, 10 of which are colored. Philadelphia: P. Blakiston's Son & Co.

THIS little book gives a simple account of the method of using the shadow test. It is clearly written and well adapted to the wants of the average student. Stress is laid almost entirely upon the practical application and little upon theoretical considerations. The appearances in emmetropia and the various forms of ametropia are described and illustrated, and their interpretation explained. The writer recommends keeping the distance between the surgeon and patient constantly at one meter. This no doubt will do fairly well for the average case, but it misses the latest development by close approximation (one-third of a meter) with special mirror and light source. Compared with the one meter method, the latter plan is analogous to the use of the high power microscope as pointed out by Dr. Jackson whose labors have so largely contributed to make skiasecopy the accurate test it is today.

T. B. S.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Treatment of Leukemia and Pernicious Anemia with Thorium X.—J. PLESCH (*Berlin. klin. Woch.*, 1912, xlix, 930) reports a case of chronic myeloid leukemia treated with thorium X. There was a rapid decrease in the number of leukocytes from 109,000 to 8,800 five days after administration of the compound. On the fifty-third day following the injection the white cells numbered 4180. More remarkable than this was the disappearance from the blood of myelocytes, which originally constituted 30 per cent. of the leukocytes. Differential count showed 59 per cent. of polynuclear neutrophiles; 5 per cent. of eosinophiles; 19 per cent. of lymphocytes; and 15 per cent. of large mononuclears, essentially a normal leukocytic formula, except for the increase of the large mononuclears. In a patient with pernicious anemia admitted to the clinic moribund, with a red count of 340,000, thorium X was injected intravenously. The next day the red count was 1,200,000. It gradually increased to 1,640,000 on the fifth day, when a second injection was given. By the thirteenth day the count was 2,270,000. On admission practically no normal erythrocytes were present in the blood; on the thirteenth day nearly all the red cells were normal in appearance. Experiments on animals have shown that one hour after an intravenous injection 38 per cent. of the thorium X is in the bone marrow. The agent deteriorates very rapidly. It is a dangerous remedy, which must be employed with great caution.

Typhoid Fever.—NICLOAE and CONSEIL (*Annales de l'Institut Pasteur*, 1912, xxvi, 332) have attempted to make use of the serum of convalescent typhoid patients, and of recovered cases in the treatment

of the disease. They have employed the serum of patients who have had a normal temperature for five to eight days. After filtration, the serum was injected in repeated doses. The duration of the disease has not been shortened, but the general condition in certain cases has improved, the nervous symptoms in particular have cleared up. The benefit has been but slight, uncertain, and in every case not at all in proportion to the difficulties of application. The records of 5 cases are given which required 685 c.c. of serum furnished by 15 convalescents. In 4 patients salvarsan was given in 50 cm. doses, with no beneficial results. In fact, Nicolae and Conseil were impressed with the danger involved. In 2 cases injections of émétique failed to show results. In view of the theory of typhoid fever as a disease of the adrenal glands, adrenalin was employed. In 11 cases 15 to 20 drops of a 1 to 100 solution were given twice a day by mouth, in 12 subcutaneously. No manifest action was observed in the circulatory disturbances, or in the progress of the disease. The abscess of fixation, after Morsly, was used repeatedly, without demonstrable effect.

A New Technique for the Diazo Reaction of Ehrlich.—K. FERI (*Wien. klin. Woch.*, 1912, xxv, 919) describes a new method of performing the diazo reaction of Ehrlich. He employs paranitrodiazobenzol sulphate, known in commercial chemistry as azophorrot P. N. The test is performed in the following manner: A few granules of azophorrot P. N. are placed in a test tube with water (tap water may be used). The tube is inverted once or twice. Enough of the reagent is thus dissolved in the cold for use in the test. The urine is treated carefully with potassium or sodium hydrate (not with ammonia) until a slight turbidity remains. The aqueous solution of azophorrot P. N. is then added. If a bright red color appears and, after shaking, the foam is red, the reaction is positive. With an intense reaction the color is cherry red. In a large series of cases tested with this method and the original technique of Ehrlich, the results corresponded invariably. The advantages of the new method are several; there is the substitution of a dry substance for the two solutions, there is no necessity for accurate mixing of the reagents, and the technique is much simplified.

Cutaneous Allergy in Gonococcal Infections.—IRONS (*Jour. Infect. Dis.*, 1912, xl, 77) notes the reactions following the subcutaneous inoculation of suspensions of killed gonococci in patients suffering from gonococcal infections. These reactions are characteristic and analogous to those seen after the injection of tuberculin and mallein in the respective diseases, local redness, swelling, and tenderness, focal intensifications, and general malaise, headache, and fever. For diagnostic purposes the author uses a "gonococci" of killed bacteria, suspended in glycerin. Inoculations were made after the method of von Pirquet with a control. In infected individuals, a papule was formed in a few hours, with surrounding hyperemia, disappearing by the third day. The reactions were classed as positive when over 5 mm. in diameter. In normal adults with the infection excluded, a papule of 1 to 2 mm. was formed. The reaction varies from day to day in the same individual. In persons recently infected the reaction is

negative, and increases gradually during the course of the disease. In the more chronic forms, such as arthritis, the degree of activity varies with the changes in the clinical course of the disease. Cutaneous reactions obtained with meningococcal and gonococcal antigens suggest a group reaction. In diagnosis, if infectious meningococcus or *Micrococcus catarrhalis* are excluded, a positive reaction is considered confirmatory evidence of a gonococcal infection.

Inclusions in the Neutrophilic Cells in Scarlatina.—DÖHLE recently described inclusions in the polynuclear neutrophiles in scarlet fever, which he considered diagnostic of the disease. His results were largely confirmed by Kretschmer. I. AHMED (*Berlin. klin. Woch.*, 1912, xlix, 1232) finds, however, that the inclusions, while frequent in scarlet fever, are by no means uncommon in other febrile diseases. Thus in 10 cases of pulmonary tuberculosis which were febrile, inclusions were found in the leukocytes in all; 5 of 10 afebrile cases of tuberculosis were also positive. A patient with tuberculous meningitis, whose blood was examined four hours antemortem, showed inclusions. In 6 cases of typhoid with high fever the result was positive. German measles furnished 1 positive case. In 2 cases of measles complicated with pneumonia no inclusions were observed, but in 2 severe uncomplicated cases of measles they were found to be present. In 2 patients with varicella without fever the result was negative, as it was in the blood of 9 healthy adults. It is evident from these findings that the inclusions are not specific for scarlatina. They may be found in febrile diseases generally.

A Source of Error in the Quantitative Determination of Enzymes in the Feces.—D. GERGANOFF (*Deutsch. med. Woch.*, 1912, xxxviii, 1130) points out the possibility of error in the quantitative determination of enzymes in the feces through the admixture of blood. Blood, whether it be from the stomach or intestines, may lead to considerable increase of the fecal ferments. (Gerganoff studied diastase particularly.) Especially intestinal hemorrhages, when large, produce a decided increase. But gastric hemorrhages, when hydrochloric acid is lacking, may lead to a similar result. When free hydrochloric acid is present in the stomach it may be concluded with reserve that a bloody stool rich in diastase is not due to gastric hemorrhage, but to bleeding from the duodenum or lower portions of the intestine. This point may prove useful in the diagnosis of a gastric ulcer or in its exclusion.

Actinomycosis Treated with Vaccines.—KENICULT and MIXTER (*Boston Med. and Surg. Jour.*, 1912, clxvii, 90) have treated with "vaccines" 8 cases of actinomycosis, 2 with abdominal, 2 with pulmonary, and 4 with cervicofacial lesions. The vaccine was prepared from pure culture grown in glucose agar. The week-old colonies were ground in salt solution and sterilized by heat and preserved in lysol. It was impossible to standardize the vaccine. Therefore treatment was begun with very small doses, which were generally increased in strength. In addition, all collections of pus were incised and drained. The thoracic cases were advanced when first seen. They grew rapidly

worse and died. The vaccine caused an immediate large increase of granules in the sputum, lasting several days. One of the abdominal cases, after drainage of an abscess in the groin has apparently completely recovered after two months of vaccine treatment. The second died after varying periods of improvement. The impression was that the acute process was held in check. Of the 4 jaw cases, 3 have recovered, and 1 is rapidly improving. It seemed to Kenicutt and Mixer that the use of vaccines in superficial actinomycosis does do good.

The Results of the Treatment of Pulmonary Tuberculosis with Rosenbach's Tuberculin.—R. KOHLER and M. PLAUT (*Zeitsch. f. klin. Med.*, 1912, lxxiv, 179) have employed Rosenbach's tuberculin in the treatment of pulmonary tuberculosis. This preparation represents one of the many attempts which have been made to obtain a less toxic substance than Koch's old tuberculin. It is a culture of tubercle bacilli inoculated with *Trichophyton holoserium album*. The latter alters (digests) proteins, and it is supposed that the toxic, labile molecules of the tubercle bacilli are attacked. The toxicity of this tuberculin is apparently about 100 times less than the old Koch's tuberculin, while the active immunizing property is undiminished in strength. Kohler and Plaut have selected 80 dispensary patients, most of whom were in the first stage, though some were in the second stage of pulmonary tuberculosis. One-half of them were treated with tuberculin, the remaining half being treated with hygienic and dietetic measures alone. The patients were carefully followed for several months. The results obtained in the group treated with Rosenbach's tuberculin were strikingly good. The disease was favorably affected in 85.4 per cent. of the cases, whereas only 36.8 per cent. of the controls improved. The result is even better than this would indicate, for the patients treated with tuberculin had not the benefit of the hygienic measures used with the controls. A gain in weight was noted in 70.2 per cent. of the patients treated with tuberculin, in 33.4 per cent. of the controls. Of the tuberculin patients, 16 had elevations of temperature when they came under treatment; in 13 the temperature became normal, in 3 it was uninfluenced. The effect of the tuberculin on the subjective symptoms of the patients was the most remarkable feature of the treatment. Many of the patients were sceptical in the beginning, and frequently complained of sore arms from the injections; it is probable that suggestion can be eliminated. Nevertheless, the cough lessened or disappeared completely; night sweats, of which the majority complained, had ceased in all but 4 cases. The appetite was greatly increased, and pains were diminished or vanished. Reactions to the tuberculin were both local and general (swelling and pain in the arm, elevation of temperature, etc.). In many instances the local signs in the lungs increased shortly after the institution of the tuberculin treatment, to improve later. The case histories are given in considerable detail, and the dosage of the tuberculin is considered.

The Gastro-intestinal Disturbances of Pernicious Anemia.—In 58 cases of pernicious anemia, FRIEDENWALD (*Boston Med. and Surg. Jour.*, 1912, clxvii, 160) has made close observations of the gastro-intestinal manifestations. Loss of appetite was observed in 38 cases,

nausea in 27, vomiting in 19, indigestion in 33, diarrhea in 20, constipation in 27. Enteroptosis was present in 21 instances, atony of the stomach in 29. In 30 cases there was absence of gastric secretion. The total acidity ranged between 8 and 14. In 9 cases analysis during a period of improvement in the blood and general health did not show a return of gastric secretion.

Trichiniasis.—The researches of ROMANOVITCH (*Annales de l'Institut Pasteur*, 1912, xxvi, 351) upon trichiniasis emphasize the advisability of daily examinations of the circulating blood after the ingestion of suspected food. The female parasite penetrates the mucous membrane of the intestine, but never deeper than the muscularis. She does not reach the mesenteric glands. The larvæ are deposited in the lymph vessels or their neighborhood, and reach the circulating blood through lymphatic channels. The larvæ can enter serous cavities, peritoneal, pleural, and pericardial, but they are destroyed rapidly. It is definitely demonstrated that the larvæ penetrate the sheath of the primitive muscle fibre. This is because here better than elsewhere, the nutritive elements are found of which it has need. In traversing the intestinal mucosa the female is accompanied by bacteria. The character of infection in the blood of man and animals infected is polymicrobial. The serum of infected rabbits becomes very toxic, as early as nine days after the ingestion. The toxicity corresponds with the intensity of the larval infestation. The animals which survive an injection of the toxic serum show great wasting. The search for antibodies is unsatisfactory, both by the method of precipitins and by complement fixation. An observed case of re-infection confirms that of other authors and emphasizes the impossibility of immunizing against a new infestation. There is no preventative or abortive treatment. Salvarsan has no effect.

Viscosity of the Blood and Its Relation to Venous Murmurs.—J. MATSUO (*Deutsch. Archiv f. klin. Med.*, 1912, cvi, 433) has examined the viscosity of the blood of a large series of healthy and anemic Japanese; at the same time hemoglobin estimates and counts of the blood cells have been made. His attention has been directed chiefly to the occurrence of anemic or hemic murmurs. He finds a *bruit de diable* almost invariably present when the viscosity is below 2.8; when the viscosity rises to 3 or 3.1 the murmur disappears. In the majority of cases the intensity of the murmur is inversely proportional to the viscosity value.

The Effect of Meat Extractives on the Utilization of Vegetable Diet.—H. WOLFF (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 66) has continued his investigations of the effect of extractives on the utilization of vegetable food. His first studies were made on dogs. The present observations were made on man. He finds (1) that persons on a vegetable diet, insufficient of itself to meet the nitrogen requirement of the body, improved greatly under the administration of 5 grams of Liebig's beef extract, the nitrogen metabolism being practically in equilibrium. The result was due partly to better utilization of the nitrogen in the food and partly to a lessened excretion of nitrogen. (2) During the

administration of the beef extract an increase of uric acid occurred in the urine. On the supposition that the nitrogen of the excess of uric acid was derived from the beef extract, then 20 per cent. of the nitrogen of the beef extract was excreted in the form of uric acid. (3) Starch was better utilized; the absorption of it increased 25 to 30 per cent. under beef extract. (4) On the fat metabolism an effect was noted in two directions: (a) The fat was more completely split, and (b) the absorption was increased. (5) A comparison of these results with those obtained on dogs suggests the conclusion that improvement of the nutrition from vegetable food follows the giving of beef extract only so long as unutilized food remains in the alimentary canal. Increasing the beef extract beyond the amount necessary to produce the desired result does not appreciably alter the metabolism.

Effect of Adrenalin, Pilocarpine, and Physostigmine on the Eosinophilic Cells.—G. SCHWENKER and H. SCHLECHT (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 77) have previously noted the marked eosinophilia both in the peripheral blood and in the lungs associated with anaphylactic shock in guinea-pigs. They have attempted to determine whether stimulation of the autonomic nervous system may be the explanation of the phenomenon. Their experiments were done on dogs and guinea-pigs. As excitants they used adrenalin, pilocarpine, and physostigmine. Following adrenalin there is a marked decrease or entire disappearance of the eosinophiles from the peripheral blood. Pilocarpine and physostigmine have no effect at all, or lead to results similar to those obtained with adrenalin. They were unable to produce a local eosinophilia, such as they have observed in the lungs in anaphylactic shock, after injection of adrenalin, pilocarpine, or physostigmine. Likewise the liver, spleen, kidneys, lymph glands, and bone marrow exhibited no increase of eosinophiles. Schwenker and Schlecht concluded that stimulation of the autonomic or sympathetic nervous system is in itself insufficient to explain the eosinophilia of anaphylactic shock in the guinea-pig.

Chlorine Content of Blood Serum in Secretory Disturbances of the Stomach.—W. ARNOLD (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 45) has examined the chlorine-content of the blood serum of patients with secretory disturbances of the stomach to determine the relationship, if any, between the chlorine-content of the serum and the hydrochloric content of the gastric juice. Serum was employed rather than whole blood, for it has been shown that it is relatively richer in chlorine and that the determinations can be made more accurately. He finds (1) that there is a change in the chlorine content of the serum with the onset of secretion of the gastric juice. (2) With anacidity and subacidity the serum constantly contains more chlorine than in hyperacidity, and at the same time the water-content is somewhat increased. (3) Some patients with anacidity whose condition cannot be differentiated clinically, presented a decreased chlorine-content of the blood serum. (4) A few cases with changing hydrochloric acid content were examined and they showed a relatively high per cent. of chlorine in the serum.

SURGERY

UNDER THE CHARGE OF

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A New Method of Gastrostomy and Esophagoplasty.—ROPKE (*Zentralbl. f. Chir.*, 1912, xxxix, 1569) says that the oblique or tortuous canal provided by the usual methods of performing a gastrostomy, sooner or later changes under tension and becomes a more or less direct fistula leading into the stomach. The feeding tube passes in and out loosely, the stomach contents escape alongside, and the surrounding skin becomes sore and inflamed. Ropke reports a case of cancer of the lower end of the esophagus in which he performed an operation devised by Jianu, who had performed it experimentally on dogs and on the human cadaver. In Ropke's case there was found a nodular tumor the size of the fist, which was inoperable. The abdomen is opened by an incision in the median line above the umbilicus. The omentum is separated along the greater curvature, the gastric arteries and veins being carefully avoided to the neighborhood of the pylorus, where they are double ligatured and divided. From the pylorus a quilted suture is introduced through both walls of the stomach up to the fundus. The suture ends just above where the left gastric artery reaches the stomach and includes between it and the greater curvature, a narrow strip of stomach about $2\frac{1}{2}$ fingers' breadth wide. This strip is left to communicate with the rest of the stomach at the cardiac end, but is cut off from the stomach in the rest of its extent by the suture. Beginning at the pyloric end this narrow strip of stomach is divided from the rest from the pyloric end up to its cardiac end, where it remains attached and is turned outward and wrapped in gauze. The quilted suture is then turned in and covered by a sero-muscular suture in its whole extent and the latter suture is continued to the cut edges of the separated flap, so that from it is made a tube leading into the stomach. The peritoneal cavity is then closed around the attachment of the new tube to the stomach where the stomach is fixed in the abdominal wound without disturbing the sutures of the new tube. The latter is now completed, a small tampon is inserted into its end and fixed by a suture, and the end of the canal is turned in over the tampon by a suture. According to the length of the new canal—in Ropke's case 22 cm.—a tunnel is made of varying length upward, under or through the pectoral muscle from the abdominal wound toward the left clavicle. With a long forceps the new stomach canal

is drawn through this tunnel. The abdominal wound is then closed completely. The upper end of the gastric canal is sutured closely to the edges of the upper end of the tunnel, its closing suture is removed, the small tampon in its end is taken out, and the edges of its mucous membrane are sutured to the skin edges of the surrounding wound. Good healing occurred. After eight days fluid and pulpy food were passed through the new canal into the stomach, and this was kept up afterward. No backflow of stomach contents occurred.

The Necessity of Suturing Incisions of the Pelvis and Ureter.—BAZY and BAZY (*Jour. d'Urolog.*, 1912, ii, 645) consider that one should not follow a uniform course in the matter of suturing the pelvis and ureter after incision into them. They do not agree with those who say that the suture ought always to be employed, any more than with those who believe that it ought never to be used. They believe that its use should depend upon the possibility or facility with which it can be employed. They are convinced that it is an excellent practice and that the results which it gives are constantly good. But as it is not absolutely necessary, it should not be attempted at the risk of compromising the success of the operation. One should avoid with care denuding the urinary ducts and separating them from the cellulose-adipose tissue surrounding them, which fortify and carry nourishing vessels to them. It is upon these tissues, rendered resistant by the irritation from the presence of the calculi, and upon them alone that one will depend to hold the suture. Under these circumstances it can be introduced easily, rapidly, and efficaciously, and it will not be followed by contractures. When the pelvis and ureter have been denuded, suture is often impossible and in such cases it will be well to cover the opening and protect the duct by a plastic flap made from the surrounding tissues. Suture should not be employed when it appears to be difficult and in consequence gives little chance of a satisfactory result, nor when it appears to be dangerous from the standpoint of the ulterior integrity of the calibre of the urinary tract. It should not be done in patients with a precarious general condition, or when after a laborious operation it seems especially important to shorten the duration of the operation. A septic condition of the urine is not a contraindication to the suture. Nevertheless, when the infection appears to be serious and a ureterotomy has been done, it will be best, in place of attempting removal of the margins, to provide drainage of the ureter, which seems to have very desirable advantages.

Cutaneous Autoplasty in the Cure of Grave Urethro-rectal Fistulæ.—MICHON (*Jour. d'Urolog.*, 1912, ii, 681) says that some urethro-rectal fistulæ are particularly grave because of the extent of the destruction of the posterior urethra and the cicatricial induration of the perineal tissues, and demand other than the ordinary procedures for their cure. Michon obtained a good result in such a case with the following operation: A small cutaneous flap is cut from the posterior median part of the scrotum, rectangular in shape, 3 cm. long, and wide enough so that with its anterior end attached to the scrotum, it can be drawn without difficulty into the perineum. It is at first left attached by its two small ends, the one anterior and the other posterior,

and the underlying scrotal wound is closed by sutures. At the end of five or six days the posterior pedicle is divided, thus giving a movable flap attached to the scrotum with good vitality. A preanal incision is made transversely and the rectum detached up to the prostate exposing both fistulous orifices. The flap is then drawn into the wound, its cutaneous surface being turned anterior and its raw surface posterior, the posterior extremity being immediately below the loss of substance in the urethra. It is then fixed in this position by catgut sutures to the urethra and lateral tissues. The adhesion is to take place only in the depth of the wound and not along the whole anterior wall. To prevent this a little rubber tissue is interposed. The wound is tamponed carefully each day to favor the attachment of the flap in its new position. When this has been accomplished, which requires at least two weeks, one begins to divide the scrotal pedicle. This is done very slowly, at intervals of several days, and one should not forget that the perineal tissues are sclerotic and that the new vessels form very slowly. Finally when the flap is divided, its upper end is adherent to the urethral orifice only. For several days the flap is pressed into the depth of the wound by the dressings toward the position it is ultimately to occupy. The perineal wound is again opened and deepened until the posterior surface of the prostate is well exposed and the inferior free end of the flap is pushed upward turning the flap on its attached end as on a hinge. It is then fixed by sutures to the posterior surface of the prostate. The perineal wound is closed except for a small drain.

Circular Resection and Suture of the Axillary Artery for Transverse Laceration by Fracture dislocation of Anatomical Neck of the Humerus.

—BUCHANAN (*Surg., Gynec. and Obst.*, 1912, xv, 648) removed a segment of the artery at the site of the laceration and reestablished its continuity by circular suture. The patient made a good recovery but has never had a distinct radial pulse and up to the time of writing has considerable spasticity and some limitation of motion at the shoulder. The small number of cases of circular arterial suture reported to this date can be accounted for in a variety of ways: as by the fear of consecutive or secondary hemorrhage; the expectation of weakening of the vessel with resultant aneurism; the idea that the operation is difficult and requires special skill or previous animal experimentation and special instruments; the belief that thrombosis is to be expected, which will put the procedure on a par with ligation; the opinion that atheroma contraindicates arterial suture; the fact that ligation, in a very large proportion of cases, is followed by development of the collateral circulation and a result equal to arterial suture. Taking up these points in detail, the following facts should be considered (1) Hemorrhage has never followed circular suture, and in but one of the reported cases of lateral suture. This is probably due to the reason that where perfect primary union is not secured by the accurate suture, thrombosis will promptly occur, which will sufficiently plug the vessel before the stitches could possibly give way. (2) Aneurysmal dilatation has never been observed after arterial suture. (3) The operation on vessels of the size of the femoral or axillary is no more difficult than many others that the general surgeon daily performs.

Animal experimentation to acquire dexterity is certainly desirable but not essential to success for the ordinary operator. Instruments required are only such as are present in every well-equipped operating room. Thrombosis undoubtedly occurs after many arterial sutures, but in the interim the sutured vessel remains patulous and performs its function until its gradual closure by a thrombosis has induced dilatation of the collateral vessels. The writer's case is but one among a number which shows that no harm may result from arteriorrhaphy in vessels markedly atheromatous. Gangrene occurs in a certain proportion of cases of ligature of main arterial trunks (stated by Wolf as 15 per cent. in the cases of axillary ligation) and certainly some of these unfortunate results can be saved by circular suture.

Results of Experiments on Kidneys with Special Reference to Decapsulation and Establishment of Collateral Circulation.—SITER (*Surg., Gynec. and Obst.*, 1912, xv, 702) did a series of experiments on cats and dogs, in which he first decapsulated one kidney and wrapped it in omentum. At a later period the abdomen was opened and the artery to this kidney tied off. Still later the animal was killed and the resulting conditions were studied. The following facts were established: The kidney increased in size upon decapsulation. The wrapping of the kidney in the omentum is immediately successful in forming a new capsule. The collateral circulation is established at the end of ten days. The collateral circulation is sufficient to allow the kidney to function properly when the renal vessels are tied off. The kidney remains much enlarged when the capsule is removed. The forming of a new capsule from the omentum prevents adhesions between the kidney and the surrounding soft parts and increases the blood supply.

Appendicular Hernia and Hernial Appendicitis.—NORRLIN (*Arch. gén. de chir.*, 1912, vi, 1303) reports 2 cases of inflamed and strangulated appendix found in the sac of a femoral hernia. According to Glogg and others, nearly 2 per cent. of all hernias have the appendix as a part of the hernial contents. In the 2 cases here reported only the appendix was found in the sac, and it is to this particular form of the condition that attention is directed. Of 21 such cases of femoral hernia reported by Honsell, 19 were in women, aged over forty years. Of 53 analogous cases reported by Glogg, 50 were in women and on the right side, and the 2 here reported were in women, aged sixty-one and seventy-one years. The strangulation of the appendicitis can be the initial lesion. All authors agree that the diagnosis of the appendix isolated in a hernial sac is very difficult. Kirmisson made the diagnosis in one case, but there were no symptoms of intestinal occlusion. Symptoms of intestinal occlusion may be absent also when Meckel's diverticulum is strangulated, in a Littre's hernia, or in the strangulation of an epiploic appendage. In operating one ought to open the abdomen at another place in order to clear up the facts and to permit a proper estimation of the condition of the lesion. Since the peritoneal cavity is opened in a hernia operation it would be an easy matter to find and remove the appendix which would be particularly advisable if it is the seat of a chronic inflammation or a foreign body. Fortunately most inguinal and femoral hernias are on the right side.

The Mechanism of Chronic Retention in Prostatics.—VIRGHI (*Jour. d'Urolog.*, 1912, ii, 823) says that this subject has properly received much attention in recent years from urologists because in the solution of the complex problem involved lies the explanation of the urinary troubles associated with hypertrophy of the prostate. All causes of a transient or inconstant character, such as reflex inhibition, median lobe, valves of the neck, etc., should be discarded from the general discussion of the mechanism of retention. They are incapable of producing phenomena of a permanent or chronic character. Diminution or disappearance of the contractility of the muscular system of the bladder does not account for the retention in hypertrophied prostate, because micturition returns to the normal after the complete removal of the prostate, which shows that the detrusor muscle never lost its functional value, since this returns as soon as the obstacle has disappeared. The prostatic obstacle can contribute to but not create the retention. The retention is due to lesions of the sphincter of the neck, causing disturbances of the function of the sphincter during micturition and an incomplete evacuation of the bladder. Retention does not occur if, notwithstanding hyperplasia of the gland, the muscular structure of the sphincter of the neck does not undergo histological alterations. The suppression of the retention and the return of spontaneous micturition, after operations on the prostate, are due to the removal of the cervical sphincter by the operation. If one destroys the sphincter of the neck alone in an hypertrophied prostate by a special operation, he can avoid the performance of a total prostatectomy in a number of cases, and at the same time cause the disappearance of the retention. Retention in false prostatics is due to lesions of the sphincter of the neck and not to a reflex inhibition.

A Contribution to the Study of Urethritis.—ROUCAYROL and RENAUD-BADET (*Jour. d'Urolog.*, 1912, ii, 835) reports with much detail a case which he summarizes as an old chronic urethritis reawakened by an attack of grippe, with the development later of an intrabicipital abscess which was incised, and in which was found the gonococcus, modified in its form and reactions. Gonococci vaccine was given and a cure obtained. The case shows that an old chronic urethritis can conceal the gonococcus in a condition of retarded life, while bacteria examinations of the urethral discharge show no trace of it. These gonococci with retarded life are susceptible, under the influence of unknown causes, of reawakening and producing complications in different parts of the body. The cause of the reawakening in this case was the grippal infection, the microbial association of which gave a new virulence to the gonococci, which had been torpid and well tolerated up to that time. The case shows also that auto-intoxication can play an important part in the treatment of gonococci infection. A local treatment may be too intensive. In deep lesions the treatment should act mechanically to provoke by irritation absorption of the microscopic elements, while the microbes are being attracted toward the surface of the lesions. If a new microbe makes its appearance in full activity, by virtue of the law of microbial associations, the gonococcus takes on new virulence, and may be capable of grave consequences. The extragenital localization of the infection appears to be

a means of defence, and the bicipital abscess in the case here reported, seemed to be an example of this kind. The results obtained with the gonococcic vaccine are much superior to those obtained with the ordinary therapy in vogue. Local treatment is effective locally in a case of gonococcic septiceemia, but it does not affect the microbes and toxins in the blood. The salts of silver introduced into the circulation furnish appreciable results, but they are not specific. The vaccine, on the contrary, especially the autogenous vaccine prepared by culture of the blood, causes with the least reaction a progressive and definite immunity against the infectious agent. It is a vigorous specific. In this case the microbe found was analogous in all points but was not the typical gonococcus.

THE RAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Articular Rheumatism with Atophan.—BENDIX (*Therapic d. Gegenwart*, 1912, liii, 301) gave atophan in doses of from 1 to 5 grams per day to 100 cases of articular rheumatism, with very good therapeutic results. The length of treatment varied from ten days to a period of several weeks. He gives a tabulated report of all the cases treated, dividing them into groups as to results obtained by the treatment. Of the 100 cases, 45 were rapidly cured. These 45 were especially acute cases with high fever and marked joint involvement. The temperature became normal in most of these patients after two or three days of treatment, and the joint manifestations disappeared a few days later. The second group comprised the cases denoted as improved, and of these there were 28. Most of these patients had very little evidence of rheumatism after the treatment, except joint pains and stiffness that recurred after discontinuance of the remedy. The third group of 27 cases was not influenced by the treatment. More than half of this group were complicated by other diseases. The rheumatism was also of more than two weeks duration, and a few salicylic acid preparations had given no relief. Bendix says his experience with atophan in articular rheumatism leads him to the conclusion that its action is extraordinarily similar to that of the salicylic acid preparations, and only slightly inferior to them. The explanation of its action can be determined only by further experimentation. Atophan is free from untoward effects even when given in large doses over long periods of time. Three grams a day are sufficient given in divided doses, and it should be administered for at least six successive days in this way unless results are obtained within

that time. In most cases which resist salicylates, atophan will give relief if not a complete cure. He recommends, therefore, the use of atophan especially for such cases.

Antityphoid Inoculation for Nurses.—SPOONER (*Jour. Amer. Med. Assoc.*, 1912, lix, 1359) has instituted antityphoid inoculation in various training schools for nurses in Massachusetts during a period of three years, and in his article relates his observations on the subject. He says that frequent injections of small amounts of a low-virulence cause slight inconvenience. They seem to produce a protection among nurses, who are eight times more liable to the disease than the average individual. Their morbidity, under ordinary conditions, is 1.4 per cent., or 19 cases among 1361. Only 2 cases developed under these conditions. Case morbidity among the uninoculated in these hospitals is nearly nine times greater than among the inoculated, subjected to similar conditions. No permanent untoward effects have arisen from over 5000 injections. The blood picture indicates a certain protection lasting at least two and one-half years. The use of this means of protection has been shown to be safe in two epidemics, and very efficient in at least one of them.

Curative and Prophylactic Inoculation for Human Tuberculosis.—FRIEDMANN (*Berlin. klin. Woch.*, 1912, xlix, 2214) writes concerning his method of treating tuberculosis. He does not give the details of the method of preparation of his material for inoculation, but indicates that it is prepared from a variety of the tubercle bacillus which was naturally free from nearly all toxic action, and which was only slightly virulent for man. Friedmann has applied his method of treatment to 1182 cases of tuberculosis of all kinds in various clinics and hospitals under the constant critical observation of many physicians. The remedy had no untoward results even when given in larger doses than necessary for therapeutic effects. He reports uniform improvement and cures in practically all the cases treated, although his statements as to the results are general, and no exact details are given. After the treatment was shown to be harmless, children constantly exposed to tuberculosis were given prophylactic injections of the remedy. A single intramuscular injection was thus given to 335 children aged from one hour to three years. All of these children have borne the inoculation, which was given over a year ago, without the least harm. These children were, at the time of this report, free from any indication of "scrofula" or tuberculosis. Guinea-pigs were injected with very large doses of the remedy without their showing any untoward effects from the inoculation. When killed years later they were found to be entirely healthy. The avirulent bacilli had been entirely absorbed, and Friedmann believes that a certain degree of immunity was produced by the injections. The animals thus immunized were able to resist severe artificial infection; the immunized animals survived on an average, 363 days, while 10 untreated controls lived only 110 days. However, all the injected animals died eventually of the tuberculosis produced by the artificial injection. Friedmann believes that the conditions of infection in man are never so menacing as in artificial laboratory infection, and he thinks his method of treat-

ment will produce permanent protection against human tuberculosis as ordinarily contracted. In the discussion by physicians who had observed Friedmann's cases, a number confirmed his statements regarding the results obtained, but others were not so favorably inclined to the remedy. Citron and Klemperer spoke against the principle of the treatment, as they thought that the use of avirulent bacilli is dangerous since they are liable at any time to become virulent. They cite Pasteur's experience with the use of an avirulent vaccine for the treatment of chicken cholera that subsequently became very virulent. The prophylactic effect of a single injection of the remedy to infants as a prophylactic measure was questioned on the ground that it could be of little benefit to infants in later life, because any prophylactic effect would only be active as long as the bacilli remain alive within the body. A number of other objections were made against accepting the remedy until more was known as to its composition.

The Treatment of Human Cancer with Intravenous Injections of Colloidal Copper.—LOEB, McCLURG, and SWEET (*Interstate Med. Jour.*, 1912, xix, 1015) give a preliminary report as to their results with intravenous injections of colloidal copper in the treatment of human cancer. They used a colloidal solution of copper prepared according to Bredig's method. Each patient received daily an intravenous injection of 300 to 400 c.c. of the solution, warmed to about body temperature. The injection was invariably followed by a rise of temperature, and frequently accompanied by a more or less severe chill. This reaction became less marked after several injections. The patients bore the injections well; their general condition improved, and pain was so much relieved that anodynes were no longer necessary. With regard to the effect upon the tumor, they say that about two to four hours after the injection hyperemia is noticeable in the tissue adjoining the tumor. This hyperemia is often accompanied by an increase of discharge from ulcerating tumors, and by an increased sensitiveness of the tumor. Hyperemia and sensitiveness gradually disappear after about fifteen injections, and a gradual necrosis and resorption of the tumor occurs. So far the retrogression has been continuous, and at least 2 cases are near a complete cure. They report 8 cases; 2 of these had internal metastases and terminated fatally. The other 6 were cases of inoperable cancer of the face, jaw, neck, and cervical glands. Most of these had been operated upon before without success. In all of these the copper injections caused a marked retrogression of the tumor. They do not express any definite opinion on the ultimate results of this method, but hope that further investigations will lead to a still wider extension of the applicability of this mode of treatment.

Administration of Antitoxin.—PARK (*Boston Med. and Surg. Jour.*, 1912, clxviii, 73) says that the dose of diphtheria antitoxin advised by the health department of New York City for purposes of immunization is 1000 units. This dose should be repeated in ten days if danger of infection still exists. The use of tetanus antitoxin as a preventive measure has given very good results. The initial dose of

tetanus antitoxin for immunization is 1500 units and this should be repeated in fifteen days if necessary. Park emphasizes the importance of giving the required amount of antitoxin promptly, and in a single dose. He says that when diphtheria antitoxin is given subcutaneously it is present in the body fluids in a small amount on the first day, but the amount of antitoxin increases and reaches its maximum on the third and fourth day after the administration. With regard to the weight of the patient as a factor in influencing the size of the dose, Park believes that there is no question that the concentration of antitoxin in the blood and not the total amount measures the effect. He urges the intravenous method of administering diphtheria antitoxin in severe cases of diphtheria. The difference during the first day in the amount of antitoxin in the blood when injected intravenously and when injected subcutaneously is very great. At the end of six hours one has, with a proper dose by the subcutaneous method, 2 units, and by the intravenous method, 20 units in each cubic centimeter of blood. As the hours pass one diminishes and the other increases, but even at the end of twenty-four hours, there are 12 units if the antitoxin is administered intravenously against 6 units if given subcutaneously. Park says he feels sure that 5000 units given intravenously has as much effect as 20,000 given subcutaneously. He has seen intravenous injections of refined antitoxin given in nearly 200 cases, with no bad effects. It is necessary to cut down on the vein in little children, but with adults and larger children this is unnecessary. Park thinks that all cases of septic diphtheria should be given the antitoxin intravenously; but in mild and early cases it is sufficient to give it subcutaneously. Intramuscular injections are absorbed in about one-half the time required by subcutaneous ones, when the serum stays in the muscle substance; but, in practice it often escapes. Park says he has often seen life saved in tetanus by intravenous injections of tetanus antitoxin. He advises the intravenous injection of 20,000 units at the very first indication of tetanus without waiting to be certain of the diagnosis. In cases where the rigidity continues after this initial dose, the injections of smaller amounts should be repeated at twelve-hour intervals for several days, although he is doubtful as to the value of repeating the injections.

Changes in the Liver after the Administration of Salvarsan.—SEVERIN and HEINRICHSORFF (*Zeitschr. f. klin. Med.*, 1912, lxxvi, 138) report 2 cases in detail that gave marked clinical evidence of liver disease simulating acute atrophy before death and at the autopsy showing evidences of marked degenerative changes in the liver. Both of these patients had received salvarsan for luetic infections, and the question was raised whether the liver changes were induced by arsenic or were the results of syphilis. They came to the conclusion that the degenerative changes in the liver in one case were due to the arsenic, and in the other were probably due to endotoxins derived from the *spirochetæ pallida*. Severin and Heinrichsdorff say that these liver changes should only be ascribed to salvarsan upon the following conditions: (1) The clinical symptoms must follow the administration of the salvarsan. (2) There must be a definite relationship between the apparent age of the lesions produced by the salvarsan and the period

of time elapsed since the administration of the remedy. (3) The more recent areas of degeneration in the liver must contain arsenic. These three conditions were fulfilled in one of the cases reported, and were lacking in the other fatal case in which syphilis could not be excluded as the cause of death.

Absorption of Arsenic Following Intramuscular Injections of Salvarsan and Neosalvarsan.—SWIFT (*Jour. Exper. Med.*, 1913, xvii, 83) says that intramuscular injection of salvarsan and neosalvarsan in rabbits always produces necrosis of the muscles. A much more intense reaction is produced by salvarsan than by neosalvarsan. The rate of absorption of arsenic following intramuscular injections of salvarsan is very slow, while following intramuscular injections of neosalvarsan between 75 and 85 per cent. of the arsenic is absorbed during the first week. The subsequent absorption is quite slow. The rate of absorption was most constant after the injection of the neutral suspensions, a little more irregular after the injection of the alkaline solution, and most irregular after the injection of the acid suspensions. This is what might be expected if the rate of absorption is dependant upon the degree of injury produced by the injection, since neutral solutions inflict the least injury. During the first week after intramuscular injections of neosalvarsan as much arsenic was absorbed as after six weeks of salvarsan. After the first week the small amount of arsenic remaining in the muscles after neosalvarsan injections was slowly absorbed, and only about 5 per cent. remained at the end of six weeks. Swift says that the solubility of neosalvarsan combined with the neutral reaction of its solution probably explains its superiority over the old form for intramuscular injections.

Benzol in the Treatment of Leukemia.—STEIN (*Wien. klin. Woch.*, 1912, xxv, 1938) reports a case of myelogenous leukemia treated with benzol, with very great benefit. This patient had been treated systematically by the Röntgen rays, and was only slightly benefited by it. The patient was a woman, aged sixty-seven years, whose leukocytes were 225,000 when the benzol treatment was begun. As a result of the treatment, according to Stein, the leukocytes fell to 6000 and the morphology of the white cells approached more nearly that of normal blood, although a differential count still showed a small percentage of myelocytes. At the same time a marked improvement in the general condition occurred, including an increase of weight and a disappearance of all the subjective symptoms. The spleen which extended below the level of the umbilicus and to the median line before the treatment, was no longer palpable when the treatment was discontinued. The benzol was given in enteric capsules for a period of six weeks, and at the end of this time the patient was given small doses of arsenic. The marked improvement as noted above occurred while the patient was on benzol alone.

Untoward By-effects with Neosalvarsan.—SIMON (*Münch. med. Woch.*, 1912, lix, 43) reports 2 cases that developed severe toxic symptoms after the administration of neosalvarsan. These symptoms were a rash; collapse, unconsciousness for several hours, and violent

headache after recovery of consciousness. Simon denotes these as angioneurotic symptoms, due to congestion or acute swelling of the brain. These severe untoward effects may be ascribed to too high dosage, considerably higher than that of salvarsan. If given in doses equivalent to those of salvarsan, no such untoward results were obtained.

PEDIATRICS

UNDER THE CHARGE OF

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Creosotal in Pediatrics.—GEORGE HUNNAEUS (*Medizin. Klinik*, 1912, viii, 1586) gives his conclusions on creosotal based on 150 cases treated with this drug. Creosotal is not unpleasant to the taste and can be given to children very easily in warm milk. It is quickly absorbed, and creosote is found on the breath and in the urine in one hour after creosotal is ingested. It imparts to the urine an olive-green tint which has no harmful significance. Creosote also appears in the bowel and is absorbed there. Creosotal has been used particularly in France in very large doses in pneumonia, with excellent results. It tends to reduce the fever but must be exhibited until the lungs are entirely clear, to avoid a reinfection. Toxic symptoms, as delirium and convulsions, usually disappear within twenty-four hours under creosotal. Broncho-pneumonia complicating measles is favorably influenced by creosotal, and Hunnaeus gives it as a prophylactic on the appearance of Koplik's spots. It is especially beneficial in chronic bronchitis, in which it improves the appetite and general strength besides its good effect locally on the lung condition. Creosotal must be given in relatively large doses, even in infants. Hunnaeus gives the following table of doses, giving the drug three times a day: Up to one year, 5 drops; two years, 10 drops; three to four years, 15 drops; five to six years, 20 drops; seven to ten years, 25 to 30 drops. The original package of creosotal by "Heyden" or "Bayer" contain the best and purest preparation. In many cases of pneumonia the drug acts almost as a specific. It is also of considerable value in pulmonary tuberculosis in children.

The Etiology of Convulsions in Early Life.—FLOYD M. CRANDALL (*Archives of Pediatrics*, 1912, xxiv, 803) brings to notice the fact that prevention of convulsions in children is vitally important, since attacks of this nature several times repeated may lead to epilepsy in later life through the formation of an insidious inclination or even habit on the part of the brain to such discharges of energy. A large number of adult epilepsies begin really in childhood and as early as the first year. Prophylaxis is therefore very important and depends on a knowledge of the etiology of the condition in any one case. In-

fancy and childhood are themselves predisposing factors on account of the disproportionate growth of the brain during this period of life, while the control of the higher centres is slight. Heredity is another predisposing cause of convulsions. This is frequently seen in certain families in which it can be traced for several generations. Tendency to convulsive disorders is often an early symptom of rachitis, an etiological factor which should always be looked for. Among the exciting causes of convulsions are the two main groups, organic and reflex. Meningitis, tumors, and hemorrhage of the brain, etc., belong to the first group. Under the second heading dentition and phimosis, while undoubtedly causing a disturbance are rarely alone the cause of convulsions. Undigested food masses in the intestinal canal, coupled with toxemia, is the most common reflex cause of convulsions. Toxic causes include uremia and the infectious diseases, especially pneumonia and pertussis. Every seizure demands a close study to determine the underlying causes, so that further attacks may be avoided by the proper treatment. The successful treatment of the attack alone is not enough, but the future of the child must be safeguarded from a repetition of the seizure, and the possible development of a cerebral habit, leading to epilepsy.

Epidemic Catarrhal Jaundice.—LEONARD GUTHRIE (*British Jour. Child. Dis.*, 1913, x, 1) reports a small epidemic of catarrhal jaundice in children. There were 10 cases in all, and they occurred during a period of three months. Eight cases were in contiguous districts. The children were aged from three to eleven years. In 3 instances more than one member of the same family were affected. In one family two sisters, in another two sisters and one brother, and in a third a brother and sister became jaundiced between a fortnight to three months of each other. The remaining 3 cases were sporadic. All the cases showed deep jaundice, clay colored stools, and bilirubinuria. The onset was accompanied by malaise, languor, and slight fever (99° to 100° F.). In several cases vomiting occurred. The duration was from three to four weeks. Bradycardia was not observed. The liver was enlarged in 6 cases and greatly so in 4, in which it extended to within one inch of the umbilicus. The liver began to subside in size on the appearance of bile in the stools, and regained the normal size in from one to two weeks. None of the patients were seriously ill at any time. The condition is probably caused by some common organism capable of giving rise to infective hepatitis. Blockage of the main duct by mechanical causes does not produce so great an enlargement of the liver as occurred in these cases. The influenza bacillus has been designated by some as the cause of the condition. Cockayne refers to the possible analogy with mumps and the metastatic swelling of the testes and pancreas, and there is a possibility that mumps, acute pancreatitis, and hepatitis may be allotropic forms of the same infection.

Tuberculosis in Children.—ERIC PRITCHARD (*Practitioner*, 1913, xc, 280), in an article on tuberculosis in children, states that it is the commonest of all diseases affecting childhood. The incidence rate rises from zero at birth to 90 per cent. at the age of fourteen years.

Children, although highly susceptible, are little liable to fatal results except during the first two years of life. The mode of infection is mostly from human sources, by direct contact, or air-born. Unboiled, contaminated cow's milk probably causes the smaller percentage of infection of the bovine type. It is a disease especially of the lymphatic system in children, and this accounts for the absence of constitutional symptoms in many cases. Enlargement of the mediastinal glands is found in 88 per cent. of all tuberculous cases coming to autopsy. Among other diagnostic signs indicating enlarged mediastinal glands, Pritchard mentions spasmodic cough without expectoration or obvious cause, and impairment of resonance to the right of the sternum at the second intercostal space. The diagnosis of the general condition rests on the consideration of the constitutional symptoms, specific tests as the von Pirquet or Moro, and investigation of the lymphatic system. The treatment is prophylactic during the first two years of life, and the maintenance of strength during the later years of childhood. Infants should be removed from an environment of open infection. Employment of the graduated cold bath, from 100° F. down to cool, and a varied and liberal proteid diet with supplemental feeding of raw beef-juice, yolk of egg, plasmon, etc., are of great value. Later in childhood it is highly important to support the strength during the debility following measles, pertussis, and chickenpox, and to remove the child to the country if possible. In treating established cases the tuberculin treatment is uncalled for in the majority of cases. It is probably of value in surface or surgical affections. The hygienic and medical treatment is best. Intestinal stasis is decidedly unfavorable to tuberculous children. Pritchard uses an emulsion of petroleum, dram j to ij, with liquor pancreatis, ℞, and calcium hypophosphite, gr. j, three times a day, for intestinal stasis. He also prefers giving calx. sulphurata for involvement of the glands of the neck, syrup of the iodide of iron for plastic infiltration and general debility, and creosote, preferably in cod-liver oil, in all pulmonary and advanced cases.

The Leukocytes at Different Age Periods.—DINA RABINOWITSCH (*Archiv f. Kinderheilkunde*, 1912, lix, 161) refers to the observation on the leukocytes in children by various investigators, most of whom agree that the total white-cell count is higher during the first three years of life than in the adult, and that the lymphocytes are much more numerous, and the neutrophiles less in number during this period than in the adult. An adjustment takes place in the number of cells of the above type until at the fifteenth year the numbers approach the adult differential count. In Carstanjen's figures from the sixth month to the fifth year the lymphocytes drop from 50 to 25 per cent., the transitional forms from 10.5 to 7.2 per cent., and the neutrophiles rise from 35.5 to 61 per cent. From the fifth to the fifteenth year Carstanjen notes very little change in the percentages. The findings of the various investigators differ in their differential counts and in the age periods in which the different cells vary in number. Rabinowitsch, therefore, made a study of the blood in 150 healthy children to determine the differential count of the leukocytes at varying ages. The total count of white cells in children aged from

one to fifteen years, except those in the first year, showed practically the same number as in adult life, or about 6000 to 7000 cells. Sex made no difference in the count. Polynuclear neutrophils increased in number with the age of the child from 30 per cent. at the first year to 70 per cent. at the fifteenth or sixteenth year. Lymphocytes showed 60 per cent. of all white cells at the first and second year, and gradually decreased with age until they reached 30 per cent. at the sixteenth year. Eosinophils averaged from 4 to 6 per cent. throughout, varying considerably in some children at the same age period. Transitional forms averaged throughout from 2 to 3 per cent. Mast cells averaged from 0.3 to 0.6 per cent., and were often absent altogether. Large mononuclear cells averaged from 1 to 3.3 per cent., and were practically the same for all ages of children.

OBSTETRICS

UNDER THE CHARGE OF

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Operation for Puerperal Septic Infection.—At the recent International Congress of Obstetrics and Gynecology, Berlin, September 9, 1912, KOBLANCK, of Berlin, read a paper in which he advocated surgical treatment of puerperal sepsis in cases where the infection became localized. It is often difficult to diagnose the location of the infection. In 44 cases of general peritonitis he had operated, and in 23 he abstained from operation. Among the 44 cases 9 recovered and 35 perished. In 15 hemolytic bacteria were found, and among these were 4 recoveries. In the second series of 23 not operated upon, 22 died, and 1 recovered. In selecting the time for operation, in 11 patients between the first and third day was chosen, and of these 3 recovered and 8 died. In 14, operation was done from the fourth to the sixth day, with 3 recoveries and 11 deaths. In 8, from the seventh to the ninth day was chosen, with 2 recoveries and 6 deaths. When the patient had been ill from ten to twenty days, there were 11 cases operated upon, with no recoveries and 11 deaths. This would indicate that the sooner operation is performed after a diagnosis can be made, the better. In 72 cases, the principle infective focus was extirpated. Among these were 11 extirpations of the uterus, with 3 recoveries and 8 deaths. Among these patients 5 had hemolytic bacteria, with 1 recovery. Extirpation of the adnexa was practised 8 times, with 5 recoveries and 3 deaths. Hemolytic bacteria were found in 4 patients, of whom 3 recovered. Metastatic abscess was operated upon 35 times, empyema 8, with 1 recovery; joint abscess 9, with 7 recoveries; abscess of the skin and muscle 18, with 13 recoveries. Extirpation of septic veins was practised 17 times; simple ligature 7 times, with 4 recoveries and 3 deaths, of whom 3 had hemolytic bac-

teria, and 2 recovered; and 10 resections of veins, with 3 recoveries and 7 deaths, of whom 8 had hemolytic bacteria, with 3 recoveries. This resection of veins was accompanied by the extirpation of the uterus and adnexa. There were 36 cases of abscesses of the parametrium, with 34 recoveries and 2 deaths; hemolytic bacteria, 8, with 7 recoveries; and 5 cases of circumscribed peritonitis, with 2 recoveries and 3 deaths, 3 having hemolytic bacteria, with 2 recoveries. His experience would indicate that septic peritonitis should be operated upon at the earliest possible moment, and that extensive operation on the genital organ is indicated in metastatic infection. The septic uterus should be removed through the abdomen. The results will be improved if operation is performed sooner.

The Influence of the Age of the Mother on the Sex of the Child.

—AHLFELD (*Monatschr. f. Geburtsh. u. Gynäk.*, 1912, Band lxxxvi, Heft 3) concludes from his investigations that the number of male children is greater than female children in those women in whom the birth of the first child occurs after the average age. While he personally is satisfied that this is accurate, he thinks it should be corroborated by further investigation.

The Topography of the Umbilicus in Mothers and Newborn Infants.

—KAKUSCHIN (*Monatschr. f. Geburtsh. u. Gynäk.*, 1912, xxxvi, Heft 3) has investigated the relative topography of the umbilicus in the newborn child and in the mother. He finds that in taking measurements from the sternum to the umbilicus, from the symphysis to the umbilicus, and from the anterior superior spine of the ilium to the umbilicus, in different individuals, that differences as great as 14 cm. are found. Women above the average age, who have not borne children have greater measurements than the average of younger women. The occurrence of childbirth does not seem to influence these measurements. During pregnancy the lower portion of the abdominal wall is greatly distended, and all measurements in multiparæ are much greater than in primiparæ. During pregnancy the greatest increase is found in the measurement from the left anterior superior spines of the ilium to the umbilicus. As the length of the trunk of the mother's body increases, the measurement from the umbilicus to the pubis is greater. In the first day after labor the measurement from the xyphoid cartilage to the symphysis grows shorter, so that it is below its average measurement in a young woman. The greater the weight of the newborn child the higher is the umbilicus in relation to the length of the body. In female children the umbilicus is relatively higher than in male children. In full term children born in breech presentation, the umbilicus is relatively higher in the body than in children born in vertex presentation.

Perforation of the Uterus following Abortion.—PUPPE (*Monatschr. f. Geburtsh. u. Gynäk.*, 1912, Band xxxvi, Heft 3) describes 2 typical cases illustrating the danger which the general practitioner often incurs in attempting to deal with septic abortion. The first patient was the mother of nine living children, who had interrupted menstruation, and was troubled with cough and chest symptoms, for which she

consulted a general practitioner. Afterward there developed a foul discharge from the vagina, for which the doctor applied a tampon. He afterward examined the patient under an anesthetic, finding the cervix slightly dilated, so that Hegar's dilators were used to open the canal. When the dilator No. 14 was introduced, some hemorrhage followed which was checked by a tampon and was supposed to come from the mucous membrane of the surface. The putrid mass was removed so far as possible from the uterus, and the patient was sent from the consulting room to her lodging. She shortly afterward died from peritonitis. On examination a large perforation in the left parametrium was present, and behind the left ovary the peritoneum had been extensively wounded. There was a small piece of placenta in the cervix. The second case was that of a woman who had borne three children, who becoming pregnant again, endeavored to interrupt the pregnancy by hot baths, and probably interference. Hemorrhage finally developed, with pain over the sacrum, and gradual impairment of health. The patient consulted a physician, who made an examination and attempted to empty the uterus by the finger. Failing this, he used a curette and placental forceps. He then irrigated the uterus with a uterine catheter. It was observed that the water used in the irrigation did not entirely return. The patient went in a cab from the doctor's office to her house. She soon after died from peritonitis. On section, the uterus had been perforated at the fundus near the insertion of the left tube. These cases draw attention to the familiar fact that in the presence of septic abortion curetting is exceedingly dangerous. Such patients should be immediately transported to hospital where, under anesthesia, they should be carefully examined. The cervix should be dilated with the finger, and if the body of the uterus is firm, the finger or a large blunt-edged curette may be carefully employed, followed by gentle irrigation and by a tampon of iodoform gauze. If the body of the uterus is soft, nothing should be introduced within its cavity. In preparing to empty the uterus, preparations should also be made for abdominal section, and if the operator fears that he has perforated the womb during his examination, the abdomen should be immediately opened. In all doubtful cases the interior of the womb should not be molested.

An Early Case of Chorio-epithelioma Uteri.—THOMPSON and STEWART (*Jour. Obst. and Gynec. British Empire*, September, 1912) report from the Leeds Infirmary the interesting case of a multipara, aged forty-five years, who had bleeding from the uterus after six weeks' amenorrhea. This continued for ten days, obliging the patient to remain in bed. A few weeks after the first hemorrhage a second one occurred during a journey, which obliged the patient to interrupt her journey, and caused her to be very anemic upon her arrival home. On examination, small pieces of vesicular mole were found in a blood clot which had passed from the vagina. The patient was very anemic, with high temperature, and offensive vaginal discharge. The uterus was enlarged, corresponding to the period of pregnancy. After curetting, the interior of the uterus felt smooth. The materials removed were vesicular mole, portions of placenta, and blood clot. Five weeks afterward the patient bled so profusely that

death seemed threatened. On examination, a spongy mass was adherent to the posterior wall of the uterus. It was thought best to remove the uterus by abdominal hysterectomy, and this was done without complications. Fourteen months after the operation the patient was in good health and free from signs of recurrence. On examining the uterus it was three times the normal size. On the posterior wall near the fundus was a soft, friable mass, in the centre of which was a shaggy growth the size of a small walnut, infiltrating the uterine muscle. The remainder of the uterine cavity was smooth. The ovaries were considerably enlarged with numerous cysts. On microscopic examination the characteristic appearance of chorio-epithelioma was present. The uterine veins were invaded not more than one-half through the uterine wall, and but one necrotic villus was present. In the tumor there was a striking preponderance of intermediate or wandering cells, with comparatively little syncytium and Langhans' cells. Masses of the latter, however, were found in the sinuses, which is considered evidence of malignancy. Both ovaries were the seat of lutein cyst formation.

GYNECOLOGY

UNDER THE CHARGE OF

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Fascial Transplantation in Vesicovaginal Fistula.—A novel method has been resorted to by SCHMID (*Zeitschr. f. gyn. Urologie*, 1913, iv, 33) in the treatment of a stubborn case of vesicovaginal fistula following a Wertheim operation for carcinoma of the uterus. The patient was aged forty-three years; the bladder was injured during the operation, and was repaired, but a large fistula resulted, which two subsequent operations failed to close. At the third attempt, Schmidt, after again freshening the edges and closing the vesical mucosa in a transverse line with catgut, inserted between the vesical and vaginal walls a rectangular piece of fascia, about 3 by 2 cm., taken from the fascia lata of the right thigh. It was fastened with one catgut suture at each corner in such a manner as completely to cover the line of suture in the bladder wall; the vaginal mucosa was then closed over it with silk in a vertical direction. On examination of the patient three months later there was found to be no leakage whatever, and good vesical control. A thickening could be felt in the anterior vaginal wall, and by cystoscopic examination a slight protuberance could be seen on the posterior wall of the bladder, reaching not quite to the interureteric fold, and evidently corresponding to the fascial flap. The mucosa was smoothly healed over this, but showed a certain amount of hyperemia in the neighborhood of the scar. Schmidt admits that the third operation might possibly have cured this case, even without the use of

a fascial transplant, but he does not think it likely, as the tissue surrounding the fistula was densely indurated, and would in all probability have retracted as in the other attempts. There is no difficulty associated with the technique of transplanting such a small piece of fascia, which is almost sure to heal well, and which certainly, in Schmidt's opinion, gives valuable extra support in cases such as the one cited.

Menstrual Disturbances of Tuberculous Origin.—The menstrual disturbances which often accompany tuberculosis, and which have usually been attributed to the consequent anemia or cachexia, are really, according to HOLLÓS (*Deutsch. med. Woch.*, 1912, xxxviii, 2407), toxic phenomena, i. e., specific manifestations of the tuberculous virus localized somewhere in the body. He thinks that an unusually early or an unusually late onset of menstruation (before the eleventh, or after the sixteenth year) is very suggestive of tuberculosis; when tuberculosis is acquired after menstruation has been established, its toxic influence is often manifested by irregularities, amenorrhea, or dysmenorrhea. Hollós thinks that these toxic phenomena stand in some relation to the degree of immunity possessed by the individual, and to the power of reaction to a given source of intoxication, basing this belief on his experience that these toxic symptoms are absent in a much larger percentage of prognostically unfavorable cases than of cases with a good prognosis, and also on his observation that the menstrual disturbances not infrequently disappear after specific treatment of the tuberculosis.

Ovarian Involvement in Epidemic Parotitis.—In contradistinction to the testicle, which, as is well known, is exceedingly frequently the seat of a metastatic infectious process in cases of mumps, very seldom has similar involvement been demonstrated in the ovary, and 2 such instances reported by BROOKS (*Jour. Amer. Med. Assoc.*, 1913, lx, 359) are therefore of interest. Both patients were multipara, aged twenty-eight and twenty-four years respectively; in the first case the parotid involvement was unilateral and comparatively slight, but accompanied by a temperature of 104°. Seven days after its onset the ovary of the same side became enlarged, very painful, and tender on examination; the symptoms subsided after a couple of days, but the next menstrual period came on ten days ahead of time, and was more profuse than normal. In the second case the parotid involvement was bilateral, and was followed in five days by very severe pelvic pain on both sides. On examination both ovaries were found enlarged to the size of large eggs, and extremely tender. Two days after this, an acute mastitis supervened, affecting both breasts, but soon subsided, as did the ovarian inflammation. Both these patients have been under observation for a period of five years or over since their attack, and in neither instance has pregnancy occurred during this time. Brooks believes that while the condition is decidedly uncommon, it probably occurs more frequently than is generally supposed, as unless the symptoms are very marked, as in the cases he reports, it is not thought of or examined for. The probable reason for the infrequency of ovarian involvement as compared with that of the testicle is that the latter is much more exposed to slight trauma, which

favors the localization of secondary infection. Judging from these cases, and the comparatively few to be found in the literature, the involvement of the ovary appears to be a benign process, undergoing spontaneous cure, though at times associated with temporary menstrual disturbances.

Differential Diagnosis Between Ascites and Ovarian Cysts.—A simple method of clearing up the diagnosis in cases of doubt between ascites or a relaxed ovarian cyst is described by DIENST (*Münch. med. Woch.*, 1912, lix, 2731). He recommends it especially to the attention of general practitioners who may under these circumstances be forced to tap in order to relieve threatening pressure symptoms, or because of the patient's refusal of exploratory operation. The test is based upon the fact that ascitic fluid always contains fibrinogen, which is precipitated by common salt, whereas this is never found in the contents of ovarian cysts. If, therefore, a small quantity of the fluid removed at the tapping is placed in a test-tube, and one-third its volume of salt added, a flocculent precipitate will form on standing, after the salt has dissolved, if the fluid is ascitic in origin. If no precipitate forms, the fluid is certainly not ascitic, and exploratory operation should be insisted on. Dienst thinks that this test has a distinct field of usefulness, for in not a few cases of ovarian cyst, the contained fluid presents all the appearances of that from an ascites, and *vice versa*, in some cases of ascites with admixture of chyle, the fluid may strongly suggest rather thin cyst-contents.

Relation of Corpus Luteum Formation to Menstruation.—In a paper published about a year ago, and reviewed in this department at that time, Fraenkel stated his belief, based on clinical observation during laparotomies, that corpus luteum formation occurs in the intermenstruum, and chiefly in the second half of this period, so that while ovulation and menstruation do not occur simultaneously, they have a direct time-relation to each other. These clinical observations have been completely confirmed by histologic studies made by MEYER and RUGE (*Zentralbl. f. Gynäk.*, 1913, xxxvi, 50) on 87 ovaries removed during hysterectomies. By comparing the ovarian findings with the menstrual histories of the patients, and with the histologic appearance of the endometrium of the corresponding uteri, Meyer and Ruge have determined that the stage of proliferation begins about eight to twelve days after the preceeding menstruation, the stage of vascularization about the fourteenth day, and that practically complete development of the corpus luteum is reached by the seventeenth day, although the cells continue to undergo some slight further increase in size up to one or two days before the beginning of the next menstruation. Involution then begins, and by the eighth day after the menstrual period—*i. e.*, by the time the new corpus luteum is ready to start development—the old one has become completely functionless, but its complete involution to a corpus albicans, with loss of all lutein cells, takes a much longer time, so that five or six degenerating corpora lutea are often found in one ovary. In case pregnancy occurs, however, the corpus luteum remains at the height of its development throughout, and by the second month can be distinguished from that of menstruation by the rich plication of the cell layer and the extensive develop-

ment of connective tissue. The actual time of follicle rupture has not as yet been determined with accuracy, but it probably occurs immediately, or at least very shortly after menstruation, which time should therefore be the most favorable for impregnation, and which usually corresponds with a period of increased *libido sexualis*.

OTOLOGY

UNDER THE CHARGE OF

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A Case of Gonorrheal Perichondritis of Both Auricles.—H. FISCHER (*Zeitschr. f. Ohrenheilkunde*, lxxi, 1-2). This unusual demonstration of gonorrheal infection as cited by Fischer was exhibited after three attacks of increasing severity as to their manifestations in a man, aged twenty-two years. The first infection, in 1906 resolved spontaneously in between eight and nine weeks without complications. The second infection, in 1907, was followed, eight days later, by painful swelling of both ankles and the right knee. The third infection, in 1909, had similarly painful consequences involving also the right wrist, shoulder, and sternoelavicular articulation, as well as several finger joints. In addition there was a sudden excess of burning and itching sensations in both auricles lasting several days, and followed by a swelling, especially pronounced at the periphery, and accompanied by circumscribed nodulated tumefactions; the auricles felt hard and thick, and were intensely painful. There was no treatment and the acute symptoms subsided in ten weeks, leaving only a moderate degree of swelling. In November, 1911, another infection, untreated because the patient was at sea, followed two weeks later by painful swelling of the auricles, and in December the case came under immediate observation and treatment which resulted, at the end of a month in relief from the acute articular symptoms, and the temperature became normal. Ten days later there was a sudden rise in the morning temperature without evidence of recurrence of articular irritation, but with a repetition, at the end of three days, of the burning and itching sensations in the auricles which had been the preliminary symptoms of the perichondritis of three years previously. In twenty-four hours both auricles had become red and swollen, especially at the periphery, and tense to the touch, which caused severe pain. In addition to the general swelling of the auricles there were on the antihelix and at the back of the outer edge, two hard purplish nodules, firm, resistant, and unfluctuating, and especially tender. Two and one-half months later the general swelling and the nodules had much decreased, but were still in evidence. The implication of the auricle in this unusual case was plainly not a dermatitis, but an inflammation of the cartilage and of the membrane, and while the local presence of gonococci was wanting, both the character of the inflammatory process, its resemblance to reported cases of perichondritis in other parts

of the body in which the exciting cause was demonstrable and the relationships of the auricular manifestation to the more severe infections, in this individual case are in favor of the inferential diagnosis.

Contributions to the Study of the Bacteriology of Acute Otitis Media Purulenta.—In the cases reported in this communication, ABERT (*Archiv f. Ohrenheilkunde* lxxxv, 251) took, for the purposes of his investigation, pus taken from the surgically opened mastoid process, in the course of the operation, not from the middle ear through the medium of the external canal, in which respect his investigation differs from many others with which the results may be compared. A bacteriological examination was made in 110 cases and, in the majority, over 90 per cent. streptococci were present, in 18 cases streptococcus alone, 19 cases almost entirely streptococcus, 73 cases of mixed infection, streptococcus in preponderance, and also saprophytes, staphylococcus, and pneumococcus. Of these 73 cases streptococcus mucosus was determined in 8 cases, in 2 cases a pure culture, 2 cases staphylococci only, and 2 cases in combination with pneumococcus; there were also 2 notable cases in which only saprophytes were found. Of the infectious diseases, in which suppurative inflammation of the middle ear is a not infrequent sequence, scarlet fever stands first, and the bacteriological examination of the observed cases gave the following result: Streptococcus in pure culture, 5; streptococcus almost entirely, 4; streptococcus mucosus, 2; streptococcus and staphylococcus, 4. The aural implication in measles was much less frequent and bacteriologically was as follows: Streptococcus in pure culture, 1; streptococcus mucosus, 1; streptococcus and rod-like bodies, 1; staphylococcus albus, 1. Of secondary otitis there were 2 cases, one following diphtheria, the other in the course of a tuberculous infection in both of which the bacteriological finding gave streptococcus and staphylococcus. There were, in addition, 6 cases of middle-ear inflammation following influenza which could not definitely be called the otitis of influenza because no influenza bacilli were determined. Burkner reports 4 cases of otitis following influenza in which careful bacteriological examination of the secretions from the middle ear were made without proving the influenza bacillus, but demonstrating in 2 cases streptococcus pyocyaneus, in 1 case streptococcus mucosus, and in the remaining case pneumococcus. From the cases cited it was evident that the streptococcus infection preponderated, the streptococcus mucosus coming next. Next in frequency were the saprophytes, and with them a rod-like body, both aerobic and anaerobic in culture closely resembling the pyocyaneus. The saprophytes were frequently associated with bacteria, streptococcus, staphylococcus, and pneumococcus, but the exact procedure in effect of these mixed infections is not yet determined, the influenza otitis is not solely referable to influenza but may be induced by other agents.

Conditions Causing Permanency and Cicatricial Closure of Perforations of the Drum-head in Childhood.—Perforations of the drum-head have a tendency to heal because of the histological structure of that compound membrane and the conditions which lead to a permanent opening are, therefore, according to B. GOMPERS (*Zeitschr. f. Kinderheilkunde*, v, No. 1), especially worthy of consideration. In

the first year of infancy large perforations of the drum-head are rarely seen, and then only in cases of lowered vitality, in hereditary syphilis, or advanced tuberculosis; occasionally large perforations are observed in cases of measles. In the second year extensive destruction of the drum-head is observed in cases of scarlet fever, and, less frequently, in cases of typhus and measles. The extent of the destruction is limited by the vital resistance, the conditions unfavorable to healing being, according to the observations of Gompers, physical impoverishment of the parents at time of procreation as a consequence of poverty, drunkenness, syphilis, diabetes, and, especially, tuberculosis. The children of such parents have poorly nourished tissues of moderate resistance and minimum power of regeneration, and in these cases are found not only extensive persistent perforations of the drum-head, but also necrotic processes in the neighboring bony structures, and continuance of the middle-ear suppuration in the chronic form. With betterment of the general condition, accompanying appropriate aural treatment, the suppurative process may be checked and even large perforations conglutinated, but with a lowering of the general condition in strength and vitality the destructive process in the drum-head continues. In the spontaneous closure of perforations, by cicatricial tissue, the inflammation which was the cause of destruction furnishes the irritative incentive to the formation of new tissue; if this inflammatory reaction is wanting, however, the perforation remains constant until a further inflammatory reaction again stimulates newgrowth; in one case a large and long persistent perforation was observed to have become closed, as the result of a new inflammation of the middle ear, consequent upon an influx of cold water. Closure of perforations of the drum-head may be induced by the application of irritating substances to the edges of the perforation but the still more valuable preventive measure in acute inflammations of the middle ear, is an early paracentesis.

Hemorrhage Accompanying Paracentesis of the Drum-head.—Paracentesis of the drum-head in cases of acute congestion of the middle ear, CARL LUDERS (*Zeitschr. f. Ohrenheilkunde*, lxi, 1-2) says, is accompanied by hemorrhage varying in degrees proportionate to the degree of congestion and the extent and location of the incision, but usually occurring spontaneously, or easily checked by moderate tamponage. When the hemorrhage is so severe as to instantly fill, and then continue to flow from the external canal, the possibility of a complication is immediately suggested, either in the form of a structural abnormality or in a constitutionally predisposing cause. In the latter instance the outflow of blood from the middle-ear immediately following the paracentesis, instead of slackening within a few seconds, continues undiminished to the extent even of extruding the attempted tamponage of the external canal, or exhibiting itself as an outflow from the nose and mouth of the blood passing from the middle ear through the channel of the tympanopharyngeal tube. The structural abnormalities contributing to the possibilities of excessive bleeding from a paracentesis are those in which the internal carotid and the jugular bulb encroach upon the lumen of the tympanum; the constitutional predisposing causes are to be found, for example, in the natural bleeders, the nephrities, and the diabetics.

Following the report of individual cases, in one of which the recurrent hemorrhages led to operation with a lethal sequence, and a review of the literature of the subject Luders draws the following conclusions: (1) In constitutional and infectious diseases the hemorrhage following a paracentesis of the drum-head may much exceed the average of the same result in uncomplicated acute congestion of the middle ear. (2) Considerable and dangerous bleeding from the ear as a consequence of paracentesis of the drum-head is exceedingly rare. Of the thousands of cases of paracentesis there are, in the literature of the subject, in addition to the 2 cases cited by Luders, but 6 others on record. (3) In all of the recorded cases of excessive hemorrhage, following paracentesis, the blood comes from the jugular bulb and not from the carotid. (4) Alteration from the ordinary procedure in paracentesis or discrimination as to the location is not indicated. (5) A considerable hemorrhage as a consequence of a paracentesis is less dangerous in itself than is the opening of a large bloodvessel into a suppurative cavity; the consequent pyemia occurred in 2 out of the 8 cases cited. The second of the 2 cases, cited by Luders, is the only one reported in which recurrent hemorrhages led to the necessity for operation, the experience in this case indicating the necessity for ligation in the case of excessive hemorrhage following paracentesis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Specific Treatment of Experimental Pneumococcus Meningitis.

—LAMAR (*Jour. Exp. Med.*, November 1, 1912), publishes the results of experimentation with a promising therapeutic measure, namely, the use of a mixture of sodium oleate, boric acid, and antiserum. It is well-known that the use of anti-pneumococcus serum alone has been disappointing, the extent of its efficacy being confined within a very short space of time, and depending apparently upon the homologous serum being employed. With regard to the mixture spoken of above, Lamar promises an early statement as to whether homologous antiserum is absolutely necessary or not. In any case the number of strains of pneumococci is not a large one, and a suitable polyvalent serum if necessary may be procurable for use. In stating his conclusions Lamar points out that virulent pneumococci injected into the cranial or spinal cavities of monkeys produced a rapidly fatal meningitis very similar to that seen in man. Homologous immune serum, if used early, may prevent infection, or may retard the course of the disease, but subsequently is powerless to save life. The mixture of sodium oleate, immune serum and boric acid, administered repeatedly

did, however, arrest infection that had already gained headway, and led to full recovery. Such a mixture is valuable not only for meningitis but also for other pneumococcic infections such as those of the joints or the serous cavities.

The Detection of Anthrax Spores in Industrial Material.—GLYNN AND LEWIS (*Jour. of Hygiene*, June, 1912) publish the results of their work, in Liverpool, upon industrial material suspected of harboring anthrax. They were successful in more than 20 per cent. of the samples in a large series, and further they were successful in finding spores in samples disinfected by the methods now in vogue, which indicate that these methods are as yet imperfect. Glynn and Lewis consider it practically impossible to completely sterilize certain industrial materials without damaging them, but they consider that the present imperfect method is much better than none at all. In the last five year period, the British Islands show 366 human cases of which 81 were fatal, with a steady increase in the number of cases developing in the agricultural community, due to the moderate but steady increase of the disease among domestic animals in the same period. The materials usually submitted for investigation are hides, wool, hair, and bones, and importations from the Malay States gave Glynn and Lewis most of their successful results. The methods usually employed in the detection of the spores are agar plate cultures or the inoculation of guinea-pigs, of which the latter is favored. Inoculations should be made in duplicate with the centrifuged deposit of watery extract, and it is a disadvantage at present insurmountable that a considerable number of animals die from the effects of pathogenic anaërobes.

Pseudoleukemia.—At the latest meeting of the German Pathological Association, a conference was devoted to so-called pseudoleukemia (*Verhandl. d. deutsch. path. Gesellsch.*, 1912), better known in our literature as Hodgkin's disease. FRAENKEL, of Hamburg, referred to the original conception of Cohnheim, and showed that in these cases there was anemia, and a relative lymphocytosis, which lymphocytosis may pass over into a definite leukemic state, and that this happens oftener than is thought. In fact, Fraenkel says, in the few cases he has sectioned, he found a true leukemic state; this he thinks may have arisen but a few days or even hours before death, in that the organs were deprived of the ability to hold back the white cells, which then came into the circulation and gave the picture of leukemia. Although the changes in pseudoleukemia are usually observable in peripheral groups of nodes, yet internal groups can also be discovered to show microscopic changes. The enlargement of the spleen, similar to that seen in leukemia, is notable, and when this is very great, Fraenkel thinks it is hardly right to call the disease pseudoleukemia, since even in cases without splenic enlargement the increasing lymphocytes can be seen in the follicles. In the definition of the disease one has to admit the impossibility of making a classification according to the groups of nodes involved, as practically any group may be affected. Further, there may be the appearance of localized masses in the liver, kidney, lung, bowel, and elsewhere, and even in the skin as lymphodermia cutis. All this is not in any sense metastatic extension. Pseudoleukemia is a systemic-disease of the lymphatic tissue of the entire

organism; variation of intensity and of site produce the varying pictures. Fraenkel rules out the cases of Mikulicz, who described symmetrical swelling of lachrymal and salivary glands as an early stage of pseudoleukemia; rather are these to be considered as an atypical tuberculosis. Similarly, he would rule out infantile status lymphaticus. To distinguish lymphosarcoma, however, is quite another matter; in fact, Fraenkel takes the stand of Virchow that lymphosarcoma and pseudoleukemia stand very close to one another. Chloroma, Fraenkel would designate as lymphatic chloroleukemia, or if the blood remains aleukemic, hyperplastic chloropseudoleukemia; not in any sense does he consider it as a true neoplastic state. Myeloma he would class as a medullary localization of pseudoleukemia; myeloma has thus no actual identity with true tumor formation. There must therefore be two forms of pseudoleukemia, the ordinarily observed lymphoid forms and the much rarer myeloid forms—a generalized, intra- and extra-medullary hyperplasia of myeloid tissue, connected with an unchanged, or not definitely leukemic blood state. Fraenkel is unwilling to admit a splenic form of myeloid pseudoleukemia. STERNBERG, of Brunn, stated at the outset, that Hodgkin's cases were of so variable a nature that we have there no secure basis for a definition of pseudoleukemia. Having dealt with a large number of diseases which have little connection with true pseudoleukemia, he comes to the question of lymphosarcoma in Kundrat's sense of the word, which he considers must be admitted to have some connection with pseudoleukemia; at least, that form of it known as hyperplastic lymphoma is to be differentiated from true sarcoma, and both it and pseudoleukemia possess in common an alteration of the general body constitution. The frequently observed generalized lymphoid hyperplasia existing in tuberculous infections, although similar to the picture of pseudoleukemia, Sternberg characterizes as a purely tuberculous phenomenon. He counts that pseudoleukemia should not be considered in any way as an early stage of lympholeukemia, or of lymphosarcomatosis, but nevertheless feels that actually it is the same process as exists in lymphatic leukemia, and it is to be distinguished from the same only if the escape of the lymphocytes into the blood stream is restrained. Sternberg would thus admit an acute generalized pseudoleukemia, and a localized pseudoleukemia, which again may be splenic or medullary, and this last not in the unlimited sense which could include Banti's disease, but merely in the restricted sense of Cohnheim and Wunderlich. In short, Sternberg groups into pseudoleukemia, lymphosarcomatosis (with the restriction that the metastases must be in the lymphoid tissue), lymphogranulomas, the multiple plasmomas, and the splenomegalies, in all of which there is a more or less universal hyperplasia of the lymphoid tissue without leukemic signs in the blood. In discussion BENDA considered that fuller clinical examination would prove that the cases of so-called pseudoleukemia in which at autopsy the blood shows leukemic signs had been insufficiently examined clinically, and he quoted a case in which diagnosis of Banti's disease had led to extirpation of the spleen and subsequent death, because the recessions of the leukemic state had not been recognized. HIRSCHFELD considers that lymphogranulomatosis would be a preferable term to pseudoleukemia. In further discussion Aschoff thought that the term pseudoleukemia should be left to clinicians, and the

pathologists should use the term aleukemie or proleukemie lymphadenia or lymphadenosis. If we were to sum up the prevailing views of the members of the Association upon the causation of hyperplasia of the lymphoid tissues, it seems to be that a certain number of the cases are definitely due to tubercle bacilli; that in a fair number of other cases Mueh's granules have been discovered, which may be considered as evidence of the presence of tubercle bacilli of some variety, probably of reduced virulence; that even where tubercle bacilli and Mueh's granules have not been found there may yet be some cases caused by the virus of tuberculosis. Definite evidence is now at hand that in cases where Mueh's granules have been found and injection made, the animals so subjected have succumbed to a low grade tuberculosis. With regard to the terminology, Asehoff's suggestion of lymphadenosis seems a very good one, and it is possible to modify such a term with the adjective aleukemie or leukemie, according to the accompanying circumstances.

Diurnal Filaria.—Through the daily press comes the information that the metamorphosis of *Filaria loa* has been discovered to occur in the salivary glands of a fly belonging to the genus *Chrysops*. The information comes by cablegram from DR. R. P. LEIPER, who is at Calabar, and this mode of transmission of news suggests the fear of supersession which has invaded even laboratories. *Filaria loa* is confined to the west coast of Africa, and its embryos are found in the blood only during the day-time, in contradistinction to those of *Filaria bancrofti*, which are found only during the night. Not a fatal disease, the infection by *Filaria loa* is common in West Africa, its best known manifestation being the so-called "Calabar swelling" which is due to the presence of the worm in the muscles and in the vicinity of the tendons, where painful swellings are set up which may interfere seriously with the function of the limb concerned. In connection with the habits of the embryos of *Filaria loa* it is interesting to note that the insect concerned is one which bites by day, suggesting a parallel with the mosquito, which is responsible for the transmission of *Filaria bancrofti*, and which bites at night.

The attention of subscribers is called to the fact that the article entitled "Tuberculin Therapy in Surgical Tuberculosis," by Thomas Wood Hastings, M.D., which appeared in the issues of this Journal for August and September, 1912, was a Mütter Lecture delivered before the College of Physicians of Philadelphia on December 9, 1910.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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ORIGINAL ARTICLES

A YEAR'S WORK IN HYSTERECTOMY.

BY JOHN B. DEAVER, M.D., Sc.D., LL.D.,

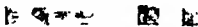
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EXPERIENCE to the physician, unlike the stern light of a ship which illuminates only that which it has passed, can more aptly be compared to the search light which may be turned into the darkness ahead lighting up both channel and obstructions.

The belief that a review of my cases of hysterectomy during the year 1911 might furnish some lessons for the future is the reason for this study. The various conditions for which the operation was done are shown in the following table:

	Cases.
Myoma	62
Myoma with sarcomatous degeneration	1
Adenomyoma	3
Carcinoma of uterus (cervix, 8; body, 6)	14
Carcinoma of Fallopian tube (primary)	1
Incomplete abortion	3
Cornual pregnancy	1
Stenosis of vagina	1
Prolapse of uterus	1
Metrorrhagia	11
Miscellaneous inflammatory conditions	11
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The operations were:

	Cases.
Complete hysterectomy	31
Vaginal hysterectomy	4
Supravaginal hysterectomy	74
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From this it is seen that myoma of the uterus furnishes the indication for the removal of this organ in rather more than half the cases. The great practical importance of this condition is emphasized by its frequency. The indications for operation in myoma of the uterus are a perennial source of strife. The radical view of the matter is that the diagnosis of the condition indicates operation. The conservative cannot be induced to recommend operation. For many years my position has been midway between these extremes. Postmortem figures compiled in large series of deaths from general causes show that about one-tenth of all women have one or more myomas of the uterus which vary in size from pea-like nodules to immense masses. In the large variety of cases these growths had nothing to do with death. It is evident therefore that there is no justification for advising operation in the cases of small symptomless fibroids, since the chances are remote that they will have any influence in shortening life. The case is entirely different when symptoms arise as a result of the growth of the tumor, of its unfavorable location, of the degeneration or accidents to which it is subject, or by reason of associated pelvic lesions.

The frequent association of other lesions in the pelvis with myoma of the uterus has impressed many observers. In the present series chronic endometritis was present in 40 cases, chronic salpingitis in 36 cases, acute salpingitis in 1, chronic metritis in 16, chronic oöphoritis in 16, and cystic disease of the ovary in 9. So frequent is it to find disease of one or more of the pelvic organs in the case of symptom-giving fibroids that the diagnosis of a troublesome fibroid is practically presumptive evidence of disease in the pelvis other than myoma of the uterus. The interesting question of the pathologic interdependence of these conditions and their relation to the clinical manifestations is too complex for general treatment or often for solution in the individual case. There is no evidence that fibroid disease of the uterus can directly cause inflammatory conditions of the adnexa, or *vice versa*. Neither is there any apparent connection between ovarian-cyst formation and the presence of fibroid tumors in the uterus.

It is fair to suppose, however, that the mechanical disturbances which follow the irregular enlargement of the uterus by myomatous disease can produce a state of lowered nutrition of the endometrium and myometrium or of the adnexæ which may permit more ready implantation of infection. Moreover, the close hormone relationship which we dimly know to exist between the various members of the genital system may be at the bottom of the association of lesions in many cases. But whether the coincidence be causal or accidental the argument for operation in these cases is strengthened by the probability of multiple lesions calling for correction.

The liability of myoma to degenerate into more serious conditions has been frequently urged as a reason for preventive removal. This argument has never appealed to me. Three hundred and forty-five cases of myoma were recently studied by Dr. Pfeiffer and myself, with special reference to degenerative changes, with the following result: Hyaline degeneration was found in 11 per cent.; cystic degeneration in 3.6 per cent.; hemorrhagic degeneration in 3.6 per cent.; calcareous degeneration in 2.4 per cent.; and sarcomatous degeneration in 1.2 per cent.

The benign forms of degeneration are not sufficiently serious to warrant preventive surgery. Sarcomatous transformation, on the other hand, is of very infrequent occurrence if the total incidence of fibroid tumors be taken into consideration.

It is one thing to say that in an operative series 1.2 per cent. of all fibroids showed sarcomatous changes and an entirely different thing to claim that the liability of myoma to degenerate into sarcoma is as 1.2 to 100, an error in logic into which many authors have fallen.

It is true, however, that myoma of the uterus predisposes to corporeal cancer of that organ. It is well known that ordinarily cancer of the cervix outnumbers cancer of the body of the uterus at least four to one. When myoma is present, however, fundal cancer is found more frequently than that of the cervix. It seems a fair assumption therefore, and one which is also suggested by the known tendency of chronic nutritional and irritative influences to excite malignant change, that a well-defined number of cases of cancer of the body of the uterus are precipitated by the presence of myoma. It is well to bear in mind therefore that the irregular uterine hemorrhage which is so frequent a result of fibroid disease may be a symptom of malignant change in the endometrium of the fundus. In this series I encountered one such case of myoma of the uterus associated with adenocarcinoma.

To my mind these risks of degenerations and of associated lesions make it desirable to remove all fibroids as soon as discovered, but it is not imperative or even advisable, even though in the best hands the risk of operation is slight. In this series there was one death due to sudden pulmonary embolism, which occurred during convalescence.

The uterus has been removed by some surgeons when no symptoms due to the tumor were present, save only a marked neurasthenia due to the patient's knowledge that she had a tumor. I would not accept this as an indication for operation save in exceptional instances.

The chief argument for removal of fibroids is presented by and not before the occurrence of symptoms. These again vary remarkably in severity and variety. Hemorrhage, chronic anemia,

malnutrition, and a weak and degenerated myocardium are not infrequent results. Pain, constant or intermittent, and of great severity, is not infrequently encountered. Pressure on the bladder, rectum, and uterus gives rise to complications. When a fibroid uterus gives trouble in any of these or other ways it should without hesitation be removed. There should be no waiting for the menopause in the vain hope of the disappearance of symptoms. This erroneous idea has been "scotched," but not entirely killed. Fibroids which give trouble before the menopause are apt to give more trouble afterward, while in many cases this trying time in a woman's life is indefinitely dragged out and made unendurably miserable. Often cases are brought into a condition of chronic invalidism through chasing this will-o'-the-wisp, and the inevitable operation is finally performed under conditions most unfavorable to the patient's recovery.

The most recent method of non-operative treatment that has been proposed for the treatment of fibroids of the uterus is the x-rays. We already know enough of the inefficiency of the x-rays in the treatment of deep-seated growths to discount the optimistic reports of some Röntgenologists. It is a certainty that this form of treatment cannot be truly curative, and we already have a surfeit of non-operative palliative methods in the treatment of surgical diseases which for the one case that is benefited causes ten to neglect timely recourse to the curative scalpel. I sincerely hope that we are not to experience in this new method a recurrence of the fallacies of the Apostoli treatment of a few years ago.

Adenoma was encountered three times during the past year. This condition, so beautifully described by Cullen, may be very difficult of diagnosis because the uterus is frequently but little enlarged and may be quite symmetrical. Free hemorrhage and grinding pain were the characteristics specially noted.

The frequency of carcinoma is illustrated by the fact that one hysterectomy in every eight was done for this disease. There is scarcely any kind of surgery that is more discouraging than this. The chief reason is the delay that occurs before these cases are brought to the surgeon. There were 8 cases of cervical cancer and 6 of cancer of the body of the uterus. In the cases of cervical cancer the average period elapsing between onset of symptoms and operation was exactly one year. In corporeal cancer the interval was greater, averaging two years and seven months. In 2 cases it was four years. This is certainly a poor showing considering the active propaganda for early diagnosis which has been in progress for several years. It is clear that these cases are brought to the surgeon not by the diagnosis, but by the development of such severe symptoms that the patient can no longer be satisfied by palliative and expectant treatment. Under conditions as they

are this disease is practically hopeless. Operation does but little more than relieve the mind of the patient and saddle the blame of the failure of treatment upon surgery. Practically the only cases of cancer of the uterus that I can claim to have cured are those that were operated upon before the disease had actually been demonstrated to be present. Until more reliable means of diagnosing carcinoma in its incipiency have been devised it will be necessary for the profession to act upon shrewd tentative diagnosis if any progress is to be made in the cure of cancer of the uterus. The chief symptom upon which we must rely in the early diagnosis is irregular, excessive, or continued bleeding. This was mentioned as one of the initial symptoms in every one of the 14 cases. Pain was present in only 3 cases, and loss of weight in 8 cases, but these as well as other occasional symptoms were not early. We must continue to insist that uterine hemorrhage should always be construed as a danger signal, and just as a lump in the breast should be considered as malignant until its innocence is proved, so should a bloody discharge from the uterus be regarded as due to carcinoma until the reverse is established. This is especially true in the cancer age, but to a less degree it applies to earlier ages, since one of my cases was aged only twenty-six years and another thirty-six years.

As practical men we must realize that the difficulty in establishing this point of view comes from two sources: (1) The disinclination of many women to secure advice upon the subject until the disturbance is marked, and the disease, if cancerous, far advanced; (2) the failure of the physician to consider the serious aspect of uterine hemorrhage until secondary symptoms make their appearance. The remedy for both these faults lies in education, and I believe that the profession is chiefly at fault. If the family physician always insisted upon discovering the cause of irregular bleeding the laity would be quick to take alarm at a symptom held in such high esteem by the profession. It is the apathy of the profession that is responsible, just as it was and still is to a large extent in its attitude toward indigestion. Just as the leaven is working in connection with abdominal diseases so it must eventually be with pelvic disturbances.

Acting in accordance with this belief I have during this year removed 13 uteri for irregular or severe hemorrhage. Not all these cases were suspected of being carcinomatous, but in several the probability was strongly considered; 11 cases showed chronic endometritis, 5 being of the hyperplastic variety and 2 showed polyp formation. In 1 the hyperplastic process was so marked as to justify the term adenoma of the endometrium. In such a case the development of cancer is to be greatly feared. In 1 case the endometrium was hyperplastic and irregular, and while the

pathologist could discover no frank signs of malignancy, he commented upon its close relation to cancer. These cases all recovered, and I feel that great good has been done by the operations, which is more than I can say of the operations in the cases diagnosed cancer, for of the ultimate results in these I am not sanguine. It is necessary to state that care must be exercised in coming to the conclusion to remove the uterus on symptoms alone, since uterine hemorrhage can occur in such a variety of less serious conditions that one may be led to do much useless surgery. I must own to having removed two uteri that were afterward discovered to show incomplete abortions. The third case of incomplete abortion upon which I operated had interstitial uterine abscesses and the operation was performed with knowledge of the condition. I was chagrined at removing a uterus for retained secundines, but with similar histories I have no doubt I would do so again, and from the long point of view it is justified, since it is better for a patient to lose her uterus unnecessarily than her life.

It is sometimes wise to remove the uterus in the course of operations for diseases that do not ordinarily indicate hysterectomy. In a case of cornual pregnancy the uterus was so eroded as to render repair uncertain and more dangerous than removal. Ordinarily adhesions and pelvic inflammatory disease give rise to conditions in the pelvis that can be remedied most expeditiously and safely by removing the uterus along with the other offending tissues. Intraligamentary cyst not infrequently defies complete removal without bringing the uterus along with it. In all such cases I prefer to leave the uterus if it can be done, as its preservation is less likely to cause weakness in the pelvic floor. Still when operative reasons indicate its removal we can now have the feeling that hysterectomy has reached a high degree of perfection and safety. The mortality in the series here reported was one-tenth of 1 per cent.

DIABETIC STANDARDS.

BY ELLIOTT P. JOSLIN, M.D.,

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WHENEVER I see the enthusiastic report of a new drug or remedy employed in the treatment of diabetes, certain cases of my own and other men come to my mind. First of all I critically examine the data relating to the new methods, and then compare the results with the cases which I have had under my eyes for years.

Gradually these cases have grown to be my *diabetic standards*. I hope to raise these standards as time goes on, and undoubtedly there are other physicians who can supply better standards; but if mine suffice to show what can be accomplished without drugs, they will have served some purpose. But each physician should have his own standard diabetic cases. This will enable him to compare the results of his past and present methods of treatment, and show him when to relinquish his own methods in favor of those of other men. Such comparisons unconsciously lead to better records of cases, and stimulate to better work.¹

The reported duration of treatment with new remedies is usually only for a period of weeks, seldom months, almost never years; for this reason I have selected cases of long duration, extending respectively over fifteen, twenty, thirteen, seven, twelve, three years and eleven months, nineteen, and six years. The shortest period during which one of these patients has been under my own observation has been five months, the longest period thirteen years. The change in the character of the urine following new methods of treatment is too often reported by a change in per cent. I have attempted to give the change in the total quantity of the sugar during the course of the case. The total quantity of carbohydrates in the diet of cases treated by drugs is rarely, if ever, accurately given. Unfortunately, I can by no means always give an accurate statement of the quantity of carbohydrates in the diet of my cases, but in many instances an accurate or nearly accurate figure will be found recorded. My standard cases are as follows:

CASE I.—Mild diabetes (glycosuria) in a man, with onset when aged thirty-three years, who became sugar-free, and remains so after fifteen years, upon a diet containing 125 grams carbohydrate.

CASE II.—Moderately severe diabetes in a man, with onset when aged fifty years, who, when aged sixty-six years became sugar-free, and succumbed to arteriosclerosis and Bright's disease at seventy, without return of sugar in the urine.

CASE III.—Moderate diabetes in a woman with onset when she was aged sixty years, who after thirteen years upon a restricted diet maintains unusual physical and mental vigor.

CASE IV.—Severe diabetes in a financier with onset when he was aged forty years, undiagnosed for four months, but later treated with extreme care and complete coöperation on the part of the patient. Duration eight and one-half years.

CASE V.—In contrast—severe diabetes with *diabetic heredity* in a bank clerk, with onset when aged thirty-seven years. He gave up the opium treatment with despair some months after

¹ As diabetic records are of necessity voluminous it will be found helpful to file them separately apart from one's general records.

Food.	Protein. Gm.	Fat. Gm.	Carbo- hydrates. Gm.	Calories.
100 grams.				Approximate.
Beef, mutton, fowl, fish (uncooked) . . .	20	5-10	..	125-170
Ham	20	25	..	300
Bacon	12	50	..	500
One egg—about 50 grams, without shell . .	6.5	5	..	75
Milk	3	4	5	70
Cream, good	3	20	3	200
Cream, very thick	3	40	3	400
Butter	1	85	..	800
Cheese	25	33	2	400
Bread	9	1	60	275
Wheat flour	12	..	75	350
Rice	8	..	80	350
Oatmeal	16	7	66	375
Potato	2	..	20	90

Vegetables lose carbohydrates in the cooking, especially if the water is changed twice. It is approximately correct to consider a mixture of those in the 5 per cent. and 6 per cent. groups as containing 3 per cent. carbohydrates or 1 gram to the ounce. Meat loses 25 per cent. water in the cooking.

Starch is better assimilated than sugar in glycosuric patients.

Potatoes and eggs of similar size weigh about the same.

One egg and 25 grams cooked (1 ounce uncooked) meat contain equal amounts of albumin, or approximately 1 gram nitrogen; 6.25 grams albumin contain 1 gram nitrogen.

One gill (3 tablespoonfuls) oatmeal weighs 36 grams (containing 1 gram nitrogen and 24 grams carbohydrate) and this if cooked amounts to (4 tablespoonfuls) 250 grams.

Approximately 80 grams glucose may be formed from 100 grams albumin.

One gram albumin contains 4 calories.

One gram carbohydrate contains 4 calories.

One gram fat contains 9 calories.

One gram alcohol contains 7 calories.

One kilogram = 2.2 pounds; 30 grams (gram) or cubic centimeters (c.c.) = 1 ounce.

A patient "at rest" requires 30 calories per kilogram body weight.

Consult the Chemical Composition of American Food Materials, Bulletin No. 28, United States Department of Agriculture, Office of Experiment Stations, Washington, D. C.

The preliminary diet often was as follows:

	Nitrogen, grams.	Total carbohy- drates. Grams.
Strict diet, meat limited to 300 grams, 3 eggs	13.0	
Vegetables in the 5, 6, 10 per cent. groups	10
Cream, 250 c.c. ($\frac{1}{2}$ pint)	1.5	5
Three small oranges or grape fruit	30
Oatmeal, 36 grams (1 gill—dry)	1.0	25
Bread made with water and without sugar, 100 grams	1.5	55
Milk, 500 c.c.	3.0	25
	20.0	150

Changes in the diet were made by the omission of milk, bread, and finally by the simultaneous reduction of oatmeal and fruit.

Even before cream was thus reached, however, the quantity of meat would be reduced to about 200 grams and fat increased.

When acidosis was present alkali was administered in the form of sodium bicarbonate or sodium citrate. Twelve to twenty-four grams daily represented the usual dose.

CASE I.—Mild Diabetes. Case No. 30. Male, born in 1864. Sugar was found in the urine upon a single occasion in 1897. There was no family history of diabetes. Measles, whooping cough, diphtheria, and typhoid fever were the only illnesses except attacks of acute duodenal indigestion at several different times and even in childhood. Indigestion persisted until 1902, when sugar was found again in the urine in one of five portions, to the amount of 0.3 per cent. Following the restriction of carbohydrates to 110 grams, sugar disappeared, save in the specimen voided after lunch, in which 0.2 per cent. was present. During 1903, 1904, and 1905, despite an increase of carbohydrates in the diet up to 125 grams, or slightly more, sugar remained absent. Upon April 14, 1906, the examination of the urine voided after lunch showed 0.5 per cent. of sugar, and that after dinner 1.1 per cent. of sugar. During the following month all specimens examined contained sugar at one or more times of the day. Beginning with 1907, sugar has remained absent from the urine in all specimens examined except in a single specimen after lunch in 1908, and again under similar conditions in 1909. The diet has increased to approximately 140 grams carbohydrates. There has been no reappearance of indigestion. Bodily weight and mental vigor have been maintained.

CASE II.—Moderate Diabetes. Case No. 354. Was at the head of a large insurance office. He was born in 1841, and gave no history of diabetes in the family. At the age of thirty-nine years disease of the heart was discovered. Except for alcohol in considerable quantities, and tobacco in excessive quantity, the previous history was unimportant. In 1891, at the age of fifty years, sugar was discovered in the urine. The patient claimed to have followed no treatment for the diabetes, but as a matter of fact, he was a most intelligent man, and inquiry has shown his diet to have been most carefully selected, conforming in general to that prescribed today for diabetic patients. From the very start he omitted sugar, and markedly increased the quantity of fat. The diet, however, was at no time rigid, being chiefly characterized by the preponderance of fatty foods and the avoidance of actually sweet articles. In 1907, at the age of sixty-six years, he was able to give up dieting altogether, for even when he took sugar it failed to appear in the urine, though incidentally albumin began to occur, and in 1910 was present in large quantities. A year later, at the age of seventy years, he died of arteriosclerosis, with accompanying nephritis, but without sugar having appeared in the urine in the interval. The last examination of the urine was as follows:

August 22, 1911. Specific gravity, 1015; reaction acid; albumin, 0.15 per cent. by Esbach; sugar none. Hyaline and granular casts and a moderate amount of pus.

CASE III.—Moderate Diabetes. Case No. 8. Showed the first symptom of diabetes in the spring of 1899 at the age of sixty years, and 5 per cent. of sugar was found in June. She had gradually lost during the preceding fifteen years 13.5 per cent. of her weight (185 to 165 pounds). Under rigid diet the urine promptly became sugar-free, and save for very transitory intervals remained so for nine years, until 1908. During 1908 and until the autumn of 1909 it returned, but except at one analysis was less than 1 per cent. In October, 1909, the sugar amounted to 4.6 per cent., and a carbuncle appeared. With prompt surgical care, vaccines, and restriction of carbohydrates, and the utilization of the oatmeal diet the sugar disappeared and the carbuncle healed promptly. But the urine did not remain permanently sugar-free, although only about 30 grams of sugar were excreted daily. In the spring of 1911 the sugar again rose at the time of an attack of lobar pneumonia, but as recovery took place and with restricted diet, the sugar disappeared. Evidently the patient could be freed from sugar, but upon a diet containing only about 30 grams of carbohydrate. This was too narrow for the patient after thirteen years of dieting, so that it was practically impossible to keep the urine free from sugar continually. Residence in a hospital for a few days in September, 1912, in order to have several teeth removed, lowered the sugar to 0.8 per cent.

Except for the brief periods of illness due to the carbuncle and pneumonia the patient remained well during all these years, and was unusually strong and vigorous for a woman of seventy-three years. I have had no patient follow directions more conscientiously. It is my present plan to prescribe a restricted diet one day in the week and to gradually increase the carbohydrate on the others up to 70 grams daily, repeating the cycle weekly.

Add to articles included in strict diet.	Mondays.	Tuesdays.	Wednesdays.	Thursdays, Fridays, Saturdays, and Sundays.
	Carbohydrates Gm.	Carbohydrates Gm.	Carbohydrates Gm.	Carbohydrates Gm.
Vegetables, 5, 6, 10 per cent. groups	10	10	10	10
Cream (250 c.c.)	5	5	5	5
Grape fruit (one-half)	5	5	5	5
Orange	$\frac{1}{2} = 5$	$1 = 10$	10
Oatmeal, 2 tablespoonfuls	12	12	12
Potato, 60 grams	12	12
Bread, 30 grams	18
Total	20	37	54	72

Sugar-free milk,² Akoll Biscuits, Alpha Biscuits, and gems made from Barker's Gluten Flour³ are allowed on all days, and an ounce of whisky, more or less, is taken.

CHART TO ILLUSTRATE CASE III.

Moderate Diabetes. Onset, 1899. Alive, 1912.

Date.	Volume, c.c.	Diacetic acid.	Sugar.		Carbo- hydrate intake, grams.	Weight in pounds.
			Per cent.	Total grams.		
June 28, 1899	1220	0	5.0	61	...	161
June 30, 1899	1720	0	3.8	65	0	
July 1, 1899	1250	0	1.0	13	10	
July 2, 1899	0	0	0	10	
Jan. 1, 1900	1200	..	0.3	4	45	174
Sept. 21, 1900	1500	..	0	0		
March 12, 1901	1415	0	1.2	17	35	176
June 1, 1901	1420	0	1.0	14		
June 5, 1903	750	..	0	0	70	150 ⁴
May 5, 1904	1000	..	0	0	100	
May 29, 1905	1000	..	0	0	130	
Aug. 14, 1906	1200	0	0	0	...	152
May 24, 1907	700	+	0	0		
May 23, 1908	740	0	0.4	3		
Nov. 10, 1908	960	0	0.8	8		
Jan. 9, 1909	1150	0	0.8	9		
Oct. 11, 1909	1290	0	3.2	41		Carbuncle
Oct. 12, 1909	860	++	2.0	19	54	
Oct. 13, 1909	700	+++	0.7	3	66	
Oct. 14, 1909	700	+++	0.2	1		
Oct. 15, 1909	760	++	0.4	3	87	
Oct. 16, 1909	910	+	0.2	4	89	
Oct. 17, 1909	800	+	0	0	76	
Oct. 18, 1909	780	0	0.2	2	78	
Oct. 21, 1909	1060	0	0	0	70	140
May 14, 1910	1400	0	1.2	17	70	155
March 13, 1911	1640	0	1.8	30		
May 14-15, 1911	925	0	3.4	31	...	Pneumonia
May 16-17, 1911	1250	0	4.0	50	65	
May 17-18, 1911	1240	0	3.4	42	65	
May 18-19, 1911	1075	0	3.0	32	60	
May 19-20, 1911	1550	0	3.8	59	60	
May 21-22, 1911	900	0	2.8	25	85	
May 22-23, 1911	600	0	2.8	17	70	
May 24-25, 1911	870	+	1.2	10	30	
May 26-27, 1911	1150	0	0.8	9		
May 28-29, 1911	890	0	0	0		
Nov. 17, 1911	1720	0	2.2	38		
Jan. 20, 1912	1520	0	2.6	40	70	
April 29, 1912	1540	0	0.6	9		
Sept. 9, 1912	2000	0	2.8	56	70	
Sept. 11, 1912	960	0	1.0	10	30	143

² Prepared by D. Whiting & Sons, Boston, Mass.³ Obtainable at 433 Broadway, Somerville, Mass.⁴ Weight, September 8.

CHART TO ILLUSTRATE CASE IV.

Severe Diabetes Onset, 1903. Died, 1912.

Date.	Volume, c.c.	Specific gravity.	Diacetic acid.	β -oxy- butyric acid. Grams.	Ammonia.		Sugar by		Carbo- hydrate intake. Grams.	Alcohol c.c.	Carbo- hydrate balance. Grams.	NaHCO ₃ Grams.	Weight. Pounds.
					Total grams.	Per cent. of nitrogen.	Fehling. Per cent.	Rotation. Grams.					
March 21, 1904	..	1041	7.8
March 30, 1904	..	1022	1.1
April 15, 1904	..	1025	0.0
March 13, 1905	3.5	..	15	..	-25
April 13-14, 1905	2000	1033	Trace	..	1.1	3.8	..	38
June 19-20, 1910	2100	1029	++	91	0	-85	24	128
July 6-7, 1910	3340	1028	+++	28.9	5.7	20.8	107	73	20	0	-45	20	126
Sept. 14-15, 1910	2560	1029	+++	32.8	4.1	20.1	63	41	20	8	-55	20	123
Dec. 7-8, 1910	3500	1025	+++	42.6	5.1	26.5	77	56	20	30	-55	20	111
March 16-17, 1911	4380	1027	+++	52.7	7.1	29.9	180	158	125	30	-55	23	76
Dec. 25-26, 1911	4700	1027	+++	54.8	6.3	35.7	188	160	135	45	+70	15	..
March 17-18, 1912	2940	1020	0	6.1	0.9	8.1	82	82	150	45	+15	5	..
March 26-27, 1912	2400	1032	0	2.6	1.3	10.8	134	115	150	45

CASE IV.—Severe Diabetes. A gentleman (Case No. 344) born March, 1863, married, financier, developed symptoms of diabetes in November, 1903, but the diagnosis was not made until March 21, 1904. He came under my observation June 27, 1910, and died of pulmonary tuberculosis in March, 1912.

There was no history of diabetes in the family. Seven uncles died of pulmonary tuberculosis.

He had suffered from measles, mumps, whooping cough, typhoid fever, scarlet fever, jaundice at approximately fifteen years of age, and malaria upon two occasions.

The record of the case is given in full because no patient has come under my observation who more carefully carried out modern dietetic treatment and also because of the extreme acidosis which disappeared with the onset of tuberculosis. In November, 1903, the patient was "run down," and in January, 1904, polydipsia appeared and he was a trifle irritable. The urine of March 21, 1904, had a specific gravity 1041, with a sugar content of 7.8 per cent. Under dietetic treatment sugar disappeared from the urine by April 15, 1904, and did not return until March 13, 1905, when the diet was somewhat relaxed. Later it again disappeared, not reappearing until October 24, 1905. It was absent throughout 1906, and present at only two of fifteen analyses during 1907. On January 24, 1908, 0.3 per cent. of sugar was present; in April of the same year Professor von Noorden found difficulty in making the urine sugar-free, despite vegetable days and oatmeal days, and from this time on the sugar was invariably present. Along with the gradual increase in acidosis, which was first noted in 1908, the diet was gradually relaxed, and apparently each time with benefit. During the latter part of December, 1911, tuberculosis appeared and the weight fell rapidly. With the appearance of the tuberculosis there was a gradual increase in the tolerance for carbohydrates and a decrease in the acidosis. Similar occurrences have been recorded by various writers.

Physical Examination: Greatest weight, 147 pounds, without clothing; June 27, 1910, 133 pounds, without clothing. Height, 6 feet. Pupils, equal and reacted to light. Teeth in excellent condition, undoubtedly due in part to cleansing by dentist every six weeks. Lungs normal. Heart, apex in mammillary line, systolic murmur at base and apex. Blood pressure, 126. Pulse rate, 96. Right kidney large and palpable throughout. Liver, spleen, and left kidney not palpable.

The reaction of the urine was acid throughout the period of our observation, and the acidosis was extreme from June, 1910, until the last few months of life. In no other case coming under my observation has the quantity of β -oxybutyric acid been greater than with this patient. It increased to over 50 grams in March, April, August, September, November, and December, 1911, and on Christmas Day was 54.8 grams. Although the amount of

nitrogen in the diet was kept at a moderate level, the ammonia was high from the first, reaching 8 grams in February, 1911, notwithstanding 20 grams of sodium bicarbonate were being taken daily. The quantity of sugar steadily rose from approximately 50 grams in June, 1910, up to 200 grams in March, 1911, but subsequently somewhat decreased, falling far below this in the spring of 1912, coincident with the presence of tuberculosis. A minus carbohydrate balance was present from June, 1910, until the last two months of life. The body weight slowly fell from 133 pounds on June 29, 1910, to 76 pounds on March 23, 1912.

CASE V.—Severe diabetes but with *hereditary taint*. This patient (Case No. 10), like the preceding and indeed like most cases of diabetes was of moderate severity at the onset. He was a bank clerk who suddenly developed diabetes at the age of thirty-seven years, March, 1898, following unusual responsibility. A brother had already died of diabetes after a few months illness at the age of fifteen years. A sister died of pulmonary tuberculosis. In October, 1899, he came under my observation discouraged and exhausted with the opium treatment which had been prescribed, having lost 45 pounds, 200 pounds to 155 pounds, which was 22.5 per cent. of his greatest weight, and with the symptoms which accompany the excretion of 233 grams of sugar (8.1 per cent.), in twenty-four hours. Under rigid dietetic treatment he became sugar-free for a few days at a time during the ensuing year, and gained 16 pounds. In November, 1901, acidosis appeared and persisted at least up to within a few months of his death, twelve and one-half years after the onset, in October, 1910. During nearly all this period he filled his position. He suffered from suppuration about the teeth, and at one time had an ulcer on the foot, but at length succumbed to pulmonary tuberculosis.

CHART TO ILLUSTRATE CASE V.

Severe Hereditary Diabetes. Onset, 1898. Died, 1910.

Date.	Volume. c.c.	Diacetic acid.	Ammonia Total. Grams.	Sugar.		Carbo- hydrate intake. Grams.	Weight. Pounds.
				Per cent.	Grams.		
March 7, 1899	1900	0.9	17		
Oct. 10, 1899	2880	0	..	8.1	233	185	
Oct. 14, 1899	1455	+	..	3.4	49	40	157
Oct. 24, 1899	2000	0	..	0	0	..	161
Nov. 10, 1899	2000	0	..	3.7	74	..	163
Nov. 14, 1899	1870	0	..	0	0	..	163
Jan. 2, 1900	1500	0	..	4.6	69	..	166
Jan. 18, 1900	1500	0	..	0	0		
May 21, 1900	1500	0	..	0	0	0	
Nov. 11, 1901	2750	+	..	4.0	110	..	161
March 9, 1908	5000	++	4.0	5.6	280	..	149 ^s

^s Weight, February 25.

CASE VI.—Severe Diabetes in Childhood. Case No. 74. A boy, aged fourteen years, developed the symptoms of diabetes in January, 1904, and a month later sugar was found in the urine. There was no diabetic heredity. In April, 1904, he came under my observation, and I saw him off and on with Dr. F. H. Thompson, of Fitchburg, who watched over the case with unusual care until the death of the patient in coma in December, 1907. The disease ran a course free from complications. The patient was sugar-free from May to December, 1904. Acidosis was present throughout. No case has come under my personal observation who developed diabetes so young and yet lived so long.

CHART TO ILLUSTRATE CASE VI.

Severe Diabetes. Onset, January, 1904. Died, December, 1907.

Date.	Volume c.c.	Acetone.	Diabetic acid.	Ammonia, total. Grams.	Sugar.		Carbo- hydrate intake grams.	Weight pounds.
					Per cent.	Grams.		
April 20, 1904	1080	+	0	..	2.5	27	..	92
May 22, 1904	1290	+++	+	..	1.2	15	..	
Dec. 21, 1904	1310	0	0	..	0.2	3	..	
Feb. 9, 1905	1470	+++	+++	..	1.1	16	..	101
Oct. 24, 1905	1860	+++	+++	..	2.9	54	..	105 ⁶
July 15, 1906	+	++	..	1.9		..	
Nov. 27, 1906	+++	+++	..	4.1	101
Jan. 10, 1907	1920	..	++++	2.9	3.4	65	..	106
April 30, 1907	2640	..	++++	4.8	3.2	03	..	104
Nov 13, 1907	2520	..	++++	3 3	3.9	98	66	

CASE VII.—Severe diabetes in youth with *diabetic heredity*. In contrast to the severe diabetes in the boy just cited, diabetic heredity was marked in Case 310, who developed diabetes in 1889 when aged seventeen years. She did not come under my observation until twenty-one years later. Her father died of kidney trouble at seventy-seven years, mother of diabetes at forty-seven years, one brother of diabetes at twenty-one years, one sister when aged about seventeen years had sugar in the urine for a period of eight months. Five brothers and sisters died in infancy, of whom one had diphtheria, and one was said to have been a blue baby. A brother and sister are well.

The first symptom of diabetes was fearful thirst while the patient was at school. The urine was voided in great quantities. Three years later sugar was demonstrated in the urine, but despite its presence the patient continued to travel and work enthusiastically. Having gone through a nurses' training school, she became a nurse, and did much hard work. The greatest volume of urine recorded

was 5400 c.c., and the specific gravity is said to have reached 1060. On March 5, 1904, the specific gravity was 1046. When examined in 1910 the patient exhibited very little thirst, no abnormal appetite. Exhaustion, insomnia, headache, poor eyesight, and pains throughout the body were the chief complaints. The hands were cracked and felt like sandpaper. There were callous spots on the feet, yet the patient said she felt "just as well as I can be." Her greatest weight was 134 pounds, and this was in 1909, but in 1910 the weight had fallen to 116 pounds. Despite the patient's contention that she was in good condition, it was obvious that she was really quite ill. The following chart shows the condition of the urine:

CHART TO ILLUSTRATE CASE VII.

Severe Hereditary Diabetes. Onset, 1889. Died, 1910.

Date.	Volume, c.c.	Specific gravity.	Diabetic acid.	β -oxybutyric acid.	Nitrogen, grams.	Ammonia, total grams.	Sugar.		Carbohydrate in diet, grams.	Carbohydrate balance, grams.	Weight of patient, lbs.
							Fehling, gms.	Rotation, gms.			
Jan. 20-21, 1910	3620	1036	0	260			
Jan. 24-25, 1910	2880	1032	0	...	15.0	2.0	...	161	185	+25	109
Feb. 1-2, 1910	2730	1025	0	...	11.6	...	96	87	130	+45	114
Feb. 7-8, 1910	2660	1026	0	...	11.4	...	113	96	165	+70	115
Feb. 9-10, 1910	2185	1023	0	...	10.6	2.9	66	57	95	+40	116
Feb. 12-13, 1910	1725	1022	Slight +	8.3	9.1	...	45	38	45	+5	117

From the urinary chart it will be seen that the patient upon taking a large quantity of carbohydrate apparently assimilated a portion, but when carbohydrates were restricted acidosis appeared. The acidosis became manifest as soon as the carbohydrates in the diet were lowered. It was for this reason unquestionably that the patient succumbed to diabetic coma soon after starting on a sea voyage. Soon after sailing she became sea-sick, and within three days diabetic coma developed, and death ensued. The explanation would appear to be that while sea-sick she was unable to take any food. As a result of no new carbohydrates being furnished to the body, the small store of carbohydrates existing, which of course was extremely small on account of the diabetes, was soon exhausted, and in the absence of the oxidation of carbohydrates acidosis became more severe, and death resulted.

CASE VIII.—Surgery in a case of moderate diabetes. Case No. 120, a married woman without diabetic heredity, was proved to have diabetes at the age of forty-seven years, in April, 1906. The urine then contained 7.2 per cent. of sugar. The date of onset of the diabetes was not accurately known, though the pruritus which had led her to a physician was first observed two months before. The patient said she had always been thirsty, for at least

ten years had passed urine frequently, and for five years had taken a pitcher of water to her bedside each night. However, seven years before an examination of the urine by a reliable physician disclosed nothing wrong. In 1904, she became aware of a fibroid. In 1906, she had lost 16.5 per cent. of her weight (230 pounds to 192 pounds). Under moderate dietetic restrictions the urine became sugar-free, but never more than for a few days, presumably because the diet was only followed with laxity. Early in January, 1908, the fibroid became so troublesome that an operation was urgent. The patient gradually was made sugar-free, and a fibroid tumor which then reached above the navel was removed by Dr. F. B. Lund. Convalescence was uneventful, and the patient remains in excellent condition. Sugar has returned, however, unlike the fortunate case of Dr. Joseph L. Miller,⁷ in which it permanently disappeared following the operation.

CHART TO ILLUSTRATE CASE VIII.

Surgery in Moderate Diabetes. Onset, 1906. Alive, 1912.

Date.	Volume, c.c.	Diabetic acid.	Sugar.		Weight of patient. Pounds.	
			Per cent.	Total grams.		
April 9, 1906 . . .	2500	0	7.2	180		
April 12, 1906 . . .	1200	Slight trace	4.7	56	198	
April 19, 1906 . . .	1125	Slight +	0.5	6	200	
May 1, 1906 . . .	1160	Slight +	0	0	199	
June 2, 1906 . . .	1160	0	0	0	198	
Feb. 17, 1907 . . .	820	Slight +	2.2	18	200	
May 17, 1907 . . .	850	++	0	0		
Feb. 22, 1908	++	0.6	Removal of uterine fibroid.
Feb. 26, 1908	0	0	0		
June 6, 1908 . . .	1260	0	0	0		
June 18, 1908 . . .	1040	0	0	0		
June 21, 1908	++	1.2			
July 28, 1908 . . .	1340	..	0	0	185	
Feb. 22, 1909 . . .	1210	0	0.5	6	185	
July 11, 1911 . . .	850	0	3.8	32		

⁷Jour. Amer. Med. Assoc., 1912, 933 (discussion).

HIGH ARTERIAL PRESSURE: HIGH PRESSURE HYPERTROPHY OF THE HEART.¹

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For a long time clinicians and pathologists in studying diseases of the circulation centred their attention almost exclusively on the heart. And even today we speak of heart failure, although we know that taken by itself such a thing is of extreme rarity. In the maintenance and control of the circulation the heart does not stand alone; it shares the responsibility with the bloodvessels, which participate actively in propelling the blood and in maintaining the blood pressure. The specific subject I wish to take out of this extensive and important field and discuss is high arterial pressure. I use this term instead of arteriosclerosis partly because the two are not synonymous, though often so used, and partly because the latter, arteriosclerosis, conveys the idea of an anatomic lesion, a terminal event best studied after death; while the former indicates at once a vital functional alteration with a direct bearing upon symptoms.

What do we mean by high arterial pressure? High arterial pressure is a relative term. Sex, age, and other factors must be taken into consideration. Up to a few years ago clinicians trusted to their fingers and eyes, but now we have fairly accurate and convenient devices by which we can determine quantitatively the amount of arterial pressure. The signal advantages of instrumental determination must be at once apparent. They are greater accuracy, standards of comparison, and ability to control treatment by recorded observations. The sphygmomanometer is to blood pressure what the hemocytometer and hemoglobinometer are to blood. Before we had them we knew of anemia, but had no definite standards and no basis for records. It is beyond the province of this paper to discuss the various instruments on the market. None is perfect; all are subject to the inevitable influence of the personal equation; but variations due to error are slight.

To know whether the blood pressure is high or not it is necessary to know the normal standards. These vary somewhat with different observers. The best records are probably those that have been obtained by careful insurance examiners, as such examiners deal more frequently than we do with healthy persons. Dr. Wolcy, of Chicago, in a study of 1000 healthy individuals, found the average to be as follows:

15 to 30 years	Blood pressure, 115 mm.
30 to 40 years	Blood pressure, 127 mm.
40 to 50 years	Blood pressure, 130 mm.

¹ An address delivered by invitation before the Wayne County Medical Society, Detroit, Michigan, May 20, 1912.

For women of the same ages the blood pressure is from 8 to 10 mm. lower. Not only age and sex, but also mental state, posture, and many other factors have an influence. Under excitement the blood pressure may rise 20 to 30 or even more millimeters. Due allowance must always be made for these variable factors.

Clinicians differ as to the exact dividing line between normal and abnormal pressure. My own feeling is that, other things being equal, a pressure over 145 is abnormal. At the age of fifty a pressure of over 150 is pathologic. This does not mean that the patient is gravely ill, but it does mean that such a patient should be kept under observation and that the cause of the rise in blood pressure should be ascertained, for when it comes to arterial disease—particularly hypertension—prevention is better and easier than cure.

As guardians of the health of our patients we are not doing our full duty. We are still too much concerned in treating the sick; a laudable purpose in itself, but one not exhausting our possibilities for good. I need not discuss the utility of preventive medicine in general. We are all agreed on that. What I have particularly in mind is personal preventive medicine. By that I mean that we should make it our duty toward our individual patients and families to guard them against such ill health as timely examinations can anticipate. To this end we should urge the men and women of over forty years of age to send urine for examination two or three times a year and to have their blood pressure taken twice a year. If we can once induce those whom we should be called upon to treat if they were ill to see the value of such examinations to themselves, our usefulness to the community and our prestige, which many new creeds and fancies have somewhat impaired, would be greatly enhanced. I see no reason why medical officers of health should not add to their preachments about communal prophylaxis, appeals for personal prophylaxis against insidious diseases of non-infectious nature which when once detected are often beyond cure.

To return to our subject: When I stated above what I considered the limits between normal and abnormal blood pressure I was giving the results of personal experience and belief. I am in the habit of looking on a pressure of from 140 to 150 in a man aged between thirty and forty years as not altogether normal if it is found on several examinations, especially if the diastolic pressure is raised 20 or 30 mm. Here I must emphasize one point to which I have already alluded: under excitement or fear, or after a heavy meal, or after exercise, the pressure rises temporarily, at times as much as 50 mm. Due allowance must be made for such transitory variations. Only when the pressure is sustained at the same level under proper conditions of testing is it significant.

When we consider the causes of high arterial pressure we enter a field with few well-defined paths. Bright's disease, particularly

the chronic interstitial variety, bears an unquestionable relationship to hypertension. But in what way the lesion of the kidney acts to bring this about is far from settled. Permanently high blood pressure is produced not only by the chronic interstitial form, the parenchymatous type also raises the blood pressure. I believe in such cases that estimation of the the blood pressure is often of great diagnostic and prognostic import. If we could explain the hypertension in nephritis we should also know the causes of the hypertrophy of the heart that is an almost constant feature of this affection. It may be remembered that the early view was that the restriction of the vascular area in the diseased and contracted kidney was responsible for the rise in blood pressure. This can scarcely be the case in view of the great adaptability of the circulation to slowly developing conditions; moreover the kidney circulation bears but a small ratio to the general vascular territory, and the local pressure restriction seems hardly capable of influencing general pressure to any marked degree.

Another view is that the disease of the kidney increases the viscosity of the blood, and hence the internal friction, and as a corollary the pressure against the vessel walls. It is quite possible that such heightened viscosity may be a factor, but the pressure is also raised under conditions in which the viscosity is presumably lessened: in chronic parenchymatous nephritis with dropsy and hydremia.

The theory that hypertension in nephritis is due to a contracted state of the vessels, the result of a generalized exaggeration of the vasomotor tonus, has had strong attractions for recent writers. It may be expressed by saying that in chronic nephritis some pressor substance circulates in the blood; either a new one or a previously existing one in increased quantity, which causes a spasm of the vessels. I see no flaw in this hypothesis except that the pressor substance is not unequivocally demonstrated. Many believe that it is adrenalin or epinephrin. While a number of investigators have found the adrenalin increased in nephritis, others have not. If there is an excessive amount in the blood, a hyperadrenalinemia, it remains yet to be explained why the adrenalin content is increased. Inasmuch as some recent investigators have found a pressor substance in the kidney itself, it is possible that through the melting down of renal tissue in Bright's disease such a substance may be liberated and taken up by the blood. Quite recently attention has been turned upon the liver in Bright's disease, as the belief is growing that the relation between that organ and the kidney is far closer than physiologists have held. It is to me not inconceivable that some of the symptoms of nephritis are connected with disturbed hepatic function. An attractive hypothesis could be erected on the theory that the kidney is an organ of internal secretion, but the paucity of facts does not warrant it. It can be

seen then how far we are from a real knowledge of the cause of hypertension in Bright's disease.

Another cause of persistent hypertension is arteriosclerosis. So much has been said and written on this subject that I shall not discuss the clinical causes or the pathology. Let me state only that arteriosclerosis is both a general and a local process. Local arteriosclerosis, which may often be intense, is not necessarily accompanied by a rise in blood pressure. Thus we may have marked calcification and beading of the accessible arteries without hypertension, and, on the other hand, I have seen a considerable number of patients with impalpable arteries whose pressure was 200 mm. or more. These are the cases that are difficult to interpret. Sometimes careful and repeated examination of the urine will show evidence of chronic interstitial nephritis: abundant urine of subnormal specific gravity with a trace of albumin and a few hyaline casts. In others the urine is entirely normal. At times the quantity is slightly increased and a few hyaline casts are found in the centrifuged specimen. I lay no stress on a sparse number of casts, especially if the urine contains crystals of uric acid and oxalate of lime.

Now it is this particular group of hypertension cases to which I have just referred that is of interest and importance; the group without notable thickening of the superficial arteries and no renal changes of importance. It is common in men and comprises, in my own experience at least, a rather large proportion of women of middle age. Not until I began to look for it did I realize how common this non-sclerotic type of hypertension is in the female sex. Both the men and women with this affection are usually robust, stout to obese, and past fifty years of age. In none of my cases in women was syphilis or alcohol a factor. In men syphilis at times plays a part, but I do not think that alcohol is to be blamed. I do not mean to say that these patients do not drink, but I wish to convey the idea that I do not consider alcohol itself an important feature in the production of high arterial tension. In the majority of cases there had been mental strain and heavy responsibility. Some of the women had reared large families under difficulties. One curious circumstance may not be without significance. Nearly all the women had come, after years of privation, to live in comparative comfort because their sons, several of them physicians and lawyers, had been successful, and had dutifully made life easy for their mothers.

The symptoms complained of were usually respiratory or gastric in nature; rarely such as to direct attention to the heart and vessels. I have no statistical tables, but I have gained the impression that one-half to two-thirds came complaining of indigestion and bloating after meals. A majority of the remainder noticed shortness of breath on exertion, which they were inclined to ascribe

to distention with gas. A few were first troubled with vertigo, with numbness and tingling of the extremities, or with ringing in the ears. The women in this group have interested me particularly because in few of them had the real nature of the affection been suspected. They had usually been treated for stomach trouble—flatulent dyspepsia or nervous indigestion.

Now what do we find on examination? The men are usually overweight, with large and solid-looking chests. They have an air of youthfulness and often much vitality. The women are large and have heavy, pendulous breasts. The heart is found enlarged, often far beyond what one would expect from either the symptoms or the physical appearance and capacity of the patient. The radials are either soft as in youth or a trifle thickened, like a thin-walled rubber tube. The temporals, which are rarely conspicuous in women, may not be abnormal. An arcus senilis is often present. The urine may not show anything of importance except a slight increase in quantity. The specific gravity will not vary much from the normal, but there is one factor of importance that I have noticed quite recently since my attention was called to it by Dr. Pratt, of Boston—namely, that these patients pass much larger amounts of urine during the night than in the daytime. I have a patient under observation at present who voids sometimes twice as much at night as in the daytime, the urine being measured separately from 8 A.M. to 8 P.M., and from 8 P.M. to 8 A.M. The blood pressure will be found high—from 190 to 260 or even more—far beyond what would be expected from an examination of the arteries.

The hypertrophy of the heart, which is always present, is not due to valvular disease. There are no endocardial murmurs except perhaps late in the course, when through loss of compensation the heart dilates and a mitral systolic murmur appears. Usually, indeed, almost without exception, the second aortic sound is much accentuated, and the first sound at the apex dull and heavy. The heart is generally regular. This type of hypertrophy is frequently overlooked, as I have had occasion to notice both in undergraduate and in postgraduate teaching. It is overlooked because many of us fail to palpate and to percuss the heart. I am inclined to believe that percussion and palpation of the heart are more important than auscultation.

Not rarely there is a systolic murmur at the aortic area without concomitant signs of aortic stenosis. The murmur indicates, I take it, sclerosis in the arch of the aorta. It is customary to make light of this murmur; justly so in the case of arteriosclerosis; but in the group with which I am dealing, in which there is no sclerosis in the peripheral vessels, the murmur, to my mind, has an important meaning. I believe the patients that have it are more liable to angina pectoris. This brings me to another important point

of interest: these high-pressure cases that do not have visible or palpable arteriosclerosis during life are particularly prone to anginal attacks, to coronary sclerosis and thrombosis. A systolic murmur at the aortic area in such a patient is ominous of an early extension of the sclerotic process from the arch into the coronary artery; its presence therefore influences the prognosis.

The blood pressure, as I have said, is high, often startlingly so, in patients whose complaints are seemingly trivial. Thus I have under my care at present a widow, aged forty-seven years, with a systolic pressure of 265, soft arteries, a perfectly regular but enlarged heart, whose chief complaint is ringing in one ear. Not a few cases have been referred to me by ophthalmologic friends who detected retinal hemorrhages. Such hemorrhages, or rather the visual disturbances dependent upon them, are often the earliest symptoms of which the patient is cognizant. Ophthalmologists have learned to recognize these high-pressure cases by means of the ophthalmoscope. Many patients, however, have normal eye-grounds.

The course of this affection, which I have been bold enough to designate *high-pressure hypertrophy*, is largely governed by the state of the heart. As long as the latter is competent the circulation is maintained at its high level, often with a minimum degree of functional disturbance. Eventually, however, the *vis a fronte* becomes too great for the *vis a tergo*, and the heart yields and dilates. The subsequent events are practically identical with those of decompensation from any other cause, and need not detain us. No doubt the lessening of the resilience of the vessels and their failure to help in the proper movement of the blood is an important contributing factor in the downward course of events.

I have been impressed with the infrequency with which high-pressure cases suffer from apoplexy. It occurs, but more often in the younger than in the older patients. Death results either from total failure of compensation or from angina pectoris, unless some intercurrent malady anticipates these two.

What is the cause of this interesting syndrome—this high-pressure hypertrophy? At first sight it looks as if there must be some pressure-raising substance in the blood. I have been hoping that some method of detecting this could be adapted to clinical application so that the theory might be tested. At present the methods are too complicated. In many cases there is, I believe, arteriosclerosis of certain important vascular territories—namely, the aortic arch and the splanchnic vessels. How sclerosis of the former raises pressure, if it does so, is a mystery. I am not sure that the ingenious hypothesis of Bittorf solves it.²

² Bittorf believes that a possible cause of high arterial pressure is degeneration of the depressor nerve or its terminations in the arch of the aorta. The depressor nerve is an afferent nerve carrying impulses to the brain, in response to which the peripheral arterial pressure is lowered through vasodilatation. When the nerve is diseased the system naturally loses this important "factor of safety."

Sclerosis of the splanchnic vessels, on account of the great area of this system, is undoubtedly capable of raising the pressure. It is likewise possible that with sclerosis of this territory some changes take place in the suprarenal glands by which the blood pressure is affected. At any rate, sclerosis of the splanchnic vessels is not uncommon, and perhaps some of the gastric distress and abdominal pains of which the patients complain may find their explanation on that basis.

I shall not dwell on the hypertension accompanying the more obvious types of arteriosclerosis. The clinical differences are not great and the diagnosis is much easier. Angina pectoris is not so common with pipe-stem peripheral arteries; apoplexy is more frequent.

TREATMENT. The treatment of hypertension is a subject of great practical importance upon which there is as little unanimity as upon most other subjects of medical practice. I have already discussed means of prevention, an object possible of accomplishment when the taking of blood pressure becomes a habit and when the laity learn to realize the importance of paying for medical advice before it is imperative to have it.

It should be borne in mind that the high pressure, like much of Nature's work in the body, is compensatory and reparative. Hence any attempt to depress the blood pressure to its normal for the individual is both irrational and harmful. All that we may safely attempt to do is to lower the blood pressure when it is excessively high to a point where symptoms cease and to keep it there. Serious consequences have followed when a pressure of 240, for example, was knocked down medicinally and precipitately to 150. Let us see what we can do to lower hypertension to a reasonable level. If we knew the direct cause we might combat it. As we do not know it we must work indirectly. First and foremost in my mind is rest, mental rest being more important than physical rest, although the latter has its place. It is astonishing what relief from the "weariness, the fever and the fret" will accomplish. Sometimes driving a patient to make a decision in a critical matter, so as to have it over with, accomplishes more than any medicine.

The diet is of importance, but more from the point of view of quantity than of quality. Many patients with hypertension have a habit of overeating, and suffer from what Sir Clifford Allbutt calls "hyperpiesis." And it may be wise to restrict somewhat the nitrogenous, more particularly the purin-containing foods. A valuable admonition is that the patient should eat a small evening meal—he will rest much better. In regard to stimulants, I am more afraid of tobacco than of alcohol, but usually restrict both, as the case may require. I do not think tea or coffee is good for these patients, a fact they often discover for themselves. The bowels must be kept open. No one remedy or measure can be employed for all cases. The salines are useful. Many persons

get comfort from a pill of phenolphthalein and rhubarb, or from the well-known compound liquorice powder. An occasional dose of calomel or blue mass serves a useful purpose. Special baths are of doubtful value, and I question particularly whether the Turkish bath so frequently employed does any good. A simple hot bath or a short electric cabinet bath may at times be of benefit, but the latter ought not to be left to the uncontrolled discretion of the patient.

Electricity in the form of the high-frequency current (autocondensation) has a growing number of advocates. My use of this is of such recent date that I have no personal opinion.

As for drugs, even the laity are familiar with the value of the nitrites, and are no longer frightened when nitroglycerin is prescribed. There are cases in which nitroglycerin fails. In these cases sodium nitrite in doses of from $\frac{1}{8}$ to 2 or even 3 grains may prove useful. Erythrol tetranitrate is a powerful vasodilator in doses of one-half grain, but often produces a painful fulness in the head, to which patients object seriously. The nitrite group of remedies is to be used only to relieve symptoms, which they often do—especially nocturnal dyspnea—in a remarkable manner. The continued use of the nitrites is of doubtful utility unless the pressure is rising, or there is angina pectoris, or marked dyspnea. In such cases they may be given over a long period in large doses.

The iodides are much in use. I give them routinely, though their method of action is unknown. Perhaps they reduce the viscosity of the blood. I prefer the sodium salt given two hours after meals, in water or milk. I find the newer iodine-containing tablets convenient, especially for persons who travel.

Digitalis might appear to be contraindicated in the cases of hypertension with which I am dealing, but strange as it may seem, many patients who are suffering from dyspnea and even from vertigo do well on small doses of digitalis. I prefer either the tincture in from 5 to 10 mm. doses three times a day, or the powdered leaves ($\frac{1}{4}$ to 1 grain).

There is one more measure in the value of which I have an abiding faith—namely, venesection. At the Philadelphia General Hospital venesection never went entirely out of use, and in the last score of years it has again become popular and is winning its way into general practice. It is safe to abstract in such cases up to a pint of blood, and if the pressure instrument is kept on the arm and the pressure controlled, we may take off 20 or 24 ounces. The relief from symptoms is often magical.

A number of European health resorts enjoy a great popularity in the treatment of hypertension and other cardiovascular conditions. Personally I doubt whether there is anything specific in their waters or in their baths; but freedom from care, regular hours, and greater frugality of living are probably the factors that achieve the good results.

A CLINICAL STUDY OF THE COAGULATION TIME OF BLOOD.

BY ROGER I. LEE, M.D.,

AND

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WE have felt for some time the need of a clinical method for determining the coagulation time of the blood which would be more satisfactory than the numerous methods previously used. The various ones which we have tried have proved unreliable in our hands. Cohen,¹ in a very complete paper on the "Coagulation Time," has discussed thirty-one methods and their modifications, and we would refer for full bibliography to his paper. Nearly all these methods fail to recognize what physiologists² have demonstrated long ago—namely, that contact with tissue markedly accelerates the coagulation time of the blood.

It is not our purpose to touch upon the various theoretic considerations of the coagulation of the blood or constituents of the blood necessary to coagulation, but mention must be made of the valuable work of Howell,³ whose theory of the coagulation of blood seems to satisfy all requirements.

Pratt,⁴ in 1903, writing from the Medical Clinic of Tübingen, embodied experimentally one of the chief principles of our method, although he used the Pratt-Grützner coagulometer. He speaks of finding the coagulation time of blood taken directly from the arm vein of man to average from six to seven minutes normally. He writes as follows in regard to it: "Coagulation time can be determined with a fair degree of accuracy by this method, but as it involves the withdrawal of the blood, directly from the veins, it was not considered feasible." At the present day, when paracentesis of the veins is done so commonly and easily, it is no longer a difficult or dangerous procedure.

Morawitz and Bierich,⁵ in 1907, published from Krehl's clinic a method of determining coagulation time in cholemic cases which closely resembles our own. Ten c.c. of blood were taken from an arm vein, 5 c.c. of this were put into test-tubes, which were watched for coagulation, and the remaining 5 c.c. were used for special examination of blood elements. Their series were apparently

¹ Archives of Internal Medicine, 1911, viii, 684.

² Howell, W. H., Text-book of Physiology, 1905, p. 418.

³ Loc. cit.

⁴ Jour. Med. Research, 1903, No. 1, x, 120.

⁵ Arch. f. experiment. Pathologie and Pharmacologie, 1907, lvi, 115.

limited to the eholemic cases and their method was not generally adopted.

Addis,⁶ in 1910, wrote of using a method of studying the coagulation time in hemophilia similar to that of Morawitz and Biérčki, except that $2\frac{1}{2}$ c.c. instead of 5 c.c. of blood were used for the test. Inversion of the tubes into which the blood was put showed the end-point.

Holmgren,⁷ in 1912, found that Schultz's method of using blood obtained by skin puncture was unsatisfactory, and therefore recommends venous puncture for obtaining blood for determination of coagulation time by a special coagulometer.

Dochez,⁸ at the Rockefeller Institute, has been using during the period of our study a method similar to ours, but more accurate and correspondingly less practical clinically. In a series of cases of pneumonia, acute and convalescent, Dochez has determined the coagulation time by withdrawing about 7 c.c. of blood from an arm vein into a syringe, emptying this blood into a carefully prepared test-tube, and then watching for the end-point by tilting the tube every thirty seconds. The test-tube is kept at 37° C.

Thus although the method to be described is not completely new, it has been used on so small a scale and in such limited series as to justify a more extended study.

Method. One c.c. of blood is withdrawn from an arm vein, using a small all glass syringe (for example, Burroughs and Welleome, 20 minims), preferably with a platinum needle, the syringe having been first sterilized and rinsed out with normal salt solution. The time at which the blood is withdrawn is noted as accurately as possible; the needle is removed and the syringe is then emptied into a small glass tube (Widal tube), about 8 mm. in diameter, which has previously been rinsed out in normal salt solution. The tube is rotated endwise every thirty seconds, and that point at which the blood no longer flows from its position but maintains its surface contour when inverted is taken as the end-point. Care must be used to exclude air bubbles, as they tend to accelerate coagulation.

Observations as to the nature of the clot and of the time and extent of its retraction have been included as an important part of the method. We have controlled nearly all our cases with the coagulation time by Hayem's⁹ method, blood being obtained by a puncture of the ear with a mechanical lancet of uniform length (5 mm.). The blood used was also collected in a Widal tube as quickly as possible, and in as nearly uniform bulk as possible (that is 1 c.c.). It usually required more than one-half minute to collect this amount even after deep puncture. Our comparative results have shown the unreliability of the ear method. For example, a

⁶ Quarterly Jour. Med., iv, 16; Jour. Path. and Bact., 1911, xv, 427.

⁷ Münch. med. Woch., October 15, 1912, No. 42, p. 2281.

⁸ Jour. Exper. Med., xvi, No. 5, p. 693.

⁹ Paris, 1889, p. 323.

case of hemophilia gave a coagulation time of fifty minutes by the arm-vein method, but blood from the ear clotted in five minutes. The blood coagulated by this method (of Hayem) very uniformly between two and five minutes, with only four exceptions—namely, purpura hæmorrhagica, family type of Hanot's cirrhosis, gallstones, with marked jaundice and hemophilia. The longest time was twelve and one-half minutes in one case of hemophilia. In all four of these cases the coagulation time by the arm-vein method was also prolonged. Our only conclusion is that if the coagulation by using the blood from the ear is over five minutes, one would also find the coagulation time by using the arm vein prolonged, but negative results are of no value.

The advantages of the arm-vein method over those ordinarily used are briefly as follows: Blood is obtained directly from the blood stream without contact with tissue or skin, which contact must enter in as a factor of varying importance in the coagulation time of blood taken by skin punctures, as has been the procedure in nearly all previous methods. It has often been found that blood flowing freely from deep punctures clots much more slowly than blood expressed from shallow punctures, apparently because of the varying proportions of blood and tissue juice.¹⁰ It is obviously difficult to make punctures every time of equal depth and in tissue of equal vascularity. Therefore the results are not strictly comparable.

Another important advantage over some of the methods described previously is the simplicity of our method, the coagulometer consisting merely of the syringe and the Widal tubes. Moreover, the end-point is usually quite definite and the element of personal equation is less than in most other methods.

After the coagulation time has been determined we still have a considerable clot to study as to its character, color, and retraction, which can hardly enter into the methods where but one or two drops are studied.

The disadvantages are as follows: One is the ratio of the amount of foreign surface to the bulk of blood. This ratio is quite large in our method, but the glass syringe and tube are as smooth and clean as possible and coated with normal salt solution. We consider that much of this disadvantage is obviated. Moreover, the fact that like all methods this method is not absolute but only relative, practically rules out the argument of surface and volume ratio.

The discomfort to the patient of puncture of a vein for the blood is slight, as a rule, and has been no more disagreeable than the ear puncture. Moreover the blood may often be obtained for the test at the same time that blood is being taken for a blood culture, Wassermann, or other tests, a larger syringe being used, and a slight error thus introduced.

¹⁰ Howell, W. H., Amer. Jour. Physiol., October 1, 1912; Text-book on Physiology, 1905, p. 418.
VOL. 145, NO. 4.—APRIL, 1913.

Temperature has an important bearing on the coagulation time, as has already been indicated by Addis,¹¹ Wright,¹² Brodie and Russell,¹³ Cohen,¹⁴ Morawitz and Lissen,¹⁵ and others.

We have studied the coagulation time in 3 cases—2 normal and 1 with gastric ulcer—at varying degrees of temperature, using water baths to maintain the temperature about the Widal tubes. The results are shown by the three curves (Fig. 1).

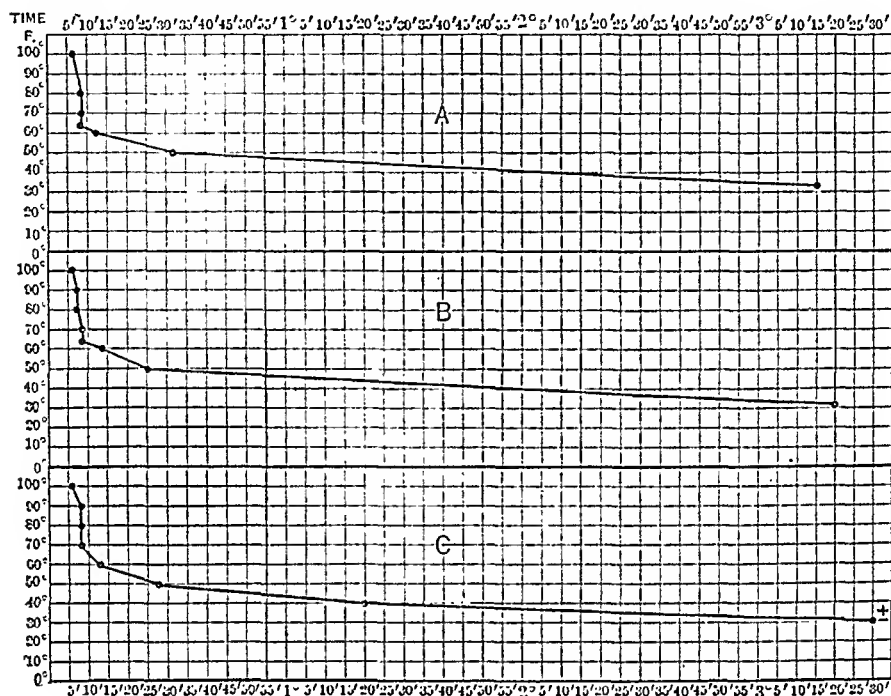


FIG. 1.—Relation of temperature and coagulation. A, healthy case; B, case of peptic ulcer; C, healthy case.

These curves indicate that if the test is done at a room temperature of 65° to 90° F., the error, although present, is within one minute, and may be neglected. However, if the temperature is below 65° or above 90° F., a warm or cool water bath should be used, maintaining a temperature of 70° F. as mean. The tests of coagulation time which we have done in summer and autumn have been in a ward with a temperature range of 65° to 90° F. The addition of an incubator, as in Doehez' method, between the degrees of 65° and 90° F. would detract from the practicability more than it would add to the accuracy.

Hinman and Sladen,¹⁶ in 1907, showed that the coagulation time of blood from the same person varied considerably with the time of day. In a case tried by our method we found little or no

¹¹ Quarterly Jour. Exper. Phys., 1908, i, 305. ¹² British Med. Jour., 1894, i, 237.

¹³ Jour. Phys., London, 1817, xxi, 403; K. Burker, Pflüger's Archiv, 1904, cii, 36.

¹⁴ Loc. cit.

¹⁵ Deut. Arch. f. klin. Med., 1908, xciv, 110.

¹⁶ Bull. Johns Hopkins Hosp., xviii, 207.

variation in the coagulation time of blood taken morning, afternoon, and evening. At 8.45 A.M., just after breakfast, the time was eight minutes; at 12 M., just before dinner, it was eight minutes; at 4.15 P.M. (before supper) it was seven and one-half minutes, and at 7.30 P.M. it was eight minutes. Thus at times during the day when coagulation would ordinarily be tested our method shows sufficient uniformity.

The results of observations of the coagulation time with the method just described on 125 cases of all kinds are shown in the accompanying table.

TABLE OF COAGULATION TIMES.

Disease.	No. of cases.	Average, arm vein.	Average, ear.	Limits, arm vein.	Limits, ear.
Normal	24	6½	3	5 - 8	2 - 4
Perniciou anemia	12	10¾	3+	5 -15	2 - 4½
Secondary anemia from gastric ulcer	4	8	3½	5 -14	2 - 5
hemorrhage	4 - 8	
Chlorosis	2	6			
Polycythemia	1	6	3		
Splenic anemia	1	15	3¾		
Myelogenous leukemia	3	6	3½	3 -10	3 - 4½
Lymphatic leukemia	1	10	3½		
Purpura hemorrhagica	1	12½	6½	10 -15	4 - 9
Hemophilia	2	52½	12½	55 -50	5 -20
Diabetes (onc with acidosis)	3	5	3	3½- 7	2 - 3
Catarrhal jaundice	3	8 (-)	3 (-)	7 - 8½	2½- 3
Cancer of liver with jaundice	4	5¼ (-)	4	5 - 6½	2½- 4
Cancer of liver without jaundice	2	8	3¼	7 - 9	3 - 3½
Gallstones with marked jaundice	2	11¾	4½	8 -15½	3½- 5½
Syphilis of liver with jaundice	1	9	3¼		
Syphilis of liver without jaundice	1	7	3		
Atrophic cirrhosis with jaundice	1	10	2		
Atrophic cirrhosis without jaundice	2	4¾	2¼	4 - 5½	2 - 2½
Hypertrophic cirrhosis with jaundice	2	14½	7	12 -17	5 - 9
Hypertrophic cirrhosis, with jaundice, family type, toxic	1	6	2½		
Infections:					
Pneumonia	6	15½	4	6½-35	3½- 4½
Typhoid	16	7+	2¾	2½-15	1½- 4½
Streptococic septicemia with arthritis, endocarditis, and pericarditis	1	11½	-	-	
Staphylococcus aureus, septicemia, and pyemia	1	13	-	-	
Brill's disease	1	2¼	1¾	-	
Acute infection	5	6	3	4 -10½	2½- 4
Gonorrheal arthritis	1	5½	-	-	
Endocarditis	4	6½	2½	2½-11½	1½- 3
Tenia	1	5	2¾	-	
Trichiniasis	1	10½	-	-	
Cardiorenals and cardiac decompensation	6	5¾	3½	4½- 6½	3¾- 5
Aortic disease	3	4½	3	4 - 5	2½- 3½
Nephritis with edema	3	9+	3	5½-14	3
Gastric ulcer (bleeding) with anemia	4	8	3¾	5 -14	
Gastric ulcer (bleeding) without anemia	1	8	-	8	
Hyperthyroidism	1	7	2½	-	
Hemoptysis in tuberculosis	2	6¾	3½	8 - 5½	

Discussion of results in clinical cases:

Normal Coagulation Time. We have found the *normal* coagulation time of blood taken by this method to be six and one-half minutes as averaged from twenty-four healthy persons, the limits being five and eight minutes. The normal average for blood from the ear was three minutes, with two- and four-minute limits, thus showing that blood obtained by skin puncture and contaminated by tissue-juice clots twice as rapidly in the normal individual as blood taken directly from the vascular system.

Accelerated Coagulation Time. Acceleration of the coagulation time (three and one-half minutes or less) was found in some cases, notably in 5 patients with typhoid fever, 4 of whom developed thrombosis. There were a number of isolated cases which showed a hastened coagulation time, including 1 of the 3 cases of myelogenous leukemia, 1 of the cases of diabetes, 1 case of typhus fever, and 1 of endocarditis.

Delayed Coagulation Time. Of the 125 cases, delay of the coagulation time occurred in 47, which may be divided into three main groups—blood diseases, jaundice, and acute infections.

Blood Diseases. Two cases of hemophilia had markedly prolonged clotting time, the longest in the series, almost an hour; both had hemorrhages. One case of purpura hæmorrhagica had delayed coagulation time, the first result being ten minutes; two and one-half weeks later the test gave fifteen minutes (the patient had grown worse steadily and died a week after the second test).

Cases of primary pernicious anemia varied considerably in coagulation time, although the average time (ten minutes) was longer than normal. Those cases that were the sickest had the most delayed coagulation time, and two cases with a coagulation time of fifteen minutes died.

One case of splenic anemia, a fatal case of acute lymphatic leukemia, and one case of myelogenous leukemia without hemorrhage showed delayed coagulation times (ten to fifteen minutes). Two cases of myelogenous leukemia were not delayed.

Liver Diseases and Jaundice. Jaundice and liver cases varied considerably in coagulation time, those with only slight jaundice being practically normal, while those with marked jaundice were often delayed. One striking case with gallstones and complete jaundice had a coagulation time of fifteen and one-half minutes, and died of secondary hemorrhage soon after operation. Another clinically similar case of gallstones, with complete jaundice, had a coagulation time of eight minutes before operation, and had no hemorrhage. Cases of syphilis and atrophic cirrhosis of liver with jaundice were above normal limits, while similar cases without jaundice were normal. Cancer of the liver even with jaundice did not retard the coagulation time in four cases. Hanot's cirrhosis

of the family type, with slight to moderate jaundice, showed in two cases a marked delay in coagulation time, twelve to seventeen minutes. Both cases (sisters) had hemorrhage. One died of spontaneous hemorrhage from mucous membranes in spite of transfusion.

Acute Infections. Of acute infectious diseases, lobar pneumonia gave the most prolonged coagulation time (average fifteen and one-half minutes). One of the six cases that was very sick had blood which took thirty-five minutes to clot. One mild case was normal (six and one-half minutes). In convalescence from pneumonia the coagulation time approaches the normal again as shown by several of our cases, especially a very severe one with a delayed time of thirty-five minutes, which became six minutes several days after crisis. This return to normal after retardation in pneumonia has been well shown by Dochez.¹⁷

Of the 16 cases of typhoid, 7 had delayed coagulation time (eight to fifteen minutes); 2 of the 7 had hemorrhages, 1 dying; 4 cases were normal, and the other 5 hastened; 4 of the latter had thrombosis, as we have noted above. Dr. Osear Richardson in an unpublished study at the Massachusetts General Hospital found that blood taken from the heart of typhoid fever patients at autopsy varied enormously in the coagulation time. In general, the cases with hemorrhage gave a prolonged coagulation time, and the cases with thrombosis an accelerated coagulation time.

One of the typhoid cases with definitely prolonged coagulation time in the acute stage of illness became normal in convalescence (thirteen minutes to seven minutes), another dropped from nine minutes to seven minutes.

Other septicemias besides pneumonia and typhoid tend to show abnormality in coagulation time. Staphylococcus aureus and streptococcic septicemia seem to delay clotting, as found in two cases (thirteen minutes and eleven and one-half minutes respectively).

Other mild acute infections showed little change in coagulation time. Three cases of acute endocarditis, one dying soon after, gave times rather shorter than normal.

Cardiac and gastric cases studied were normal. Severe nephritis gave in one case a definitely prolonged coagulation time (fourteen minutes), and in another, a fatal case, with marked edema, a coagulation time of eight minutes.

Hemoptysis in tuberculosis in two cases was not accompanied by prolonged coagulation time.

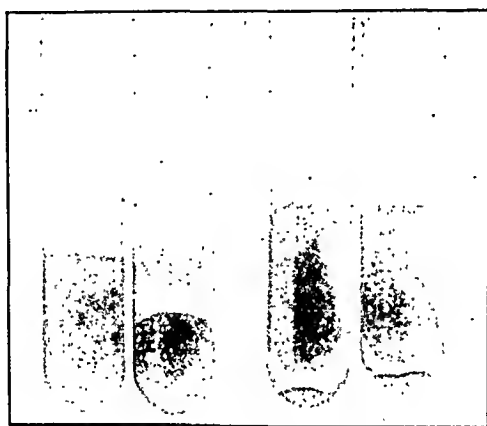
Menstruation in 3 cases did not prolong the coagulation time. In 1 case with nose bleed the coagulation time was delayed during menstruation; 250 cases tested by Keller¹⁸ during, before, and

¹⁷ Loc. cit.

¹⁸ Arch. f. Gyn., Part 3, xcvi, 540.

after menstruation showed no change in coagulation time. Pregnancy and menopause he also found did not effect the coagulation time.

In general, the coagulation time corresponded closely to the clinical picture of hemorrhage. The test was of distinct prognostic value in cases of jaundice undergoing operation. In pernicious anemia and certain other blood diseases a further delay in coagulation time was synchronous, with aggravation of symptoms. In the acute infections, excluding typhoid, the more severe infections seemed to be associated with a more delayed coagulation time. In typhoid fever there seemed to be a distinct parallelism between thrombosis and hemorrhage and the coagulation time. This question must be subjected to further study.



1 2 3 4

FIG. 2.—1, normal clot before retraction; 2, hemophilic clot before retraction; 3, normal clot after retraction; 4, hemophilic clot after retraction.

The study of the nature and retraction of the clot has been interesting. There have been 35 cases out of the 125 which we have tested in which there has been more or less settling of the red blood corpuscles. Of these, 31 have had definitely long coagulation times and 3 others on the border-line of normal. The most marked settling of corpuscles occurred in 6 cases, in which the coagulation time was twice normal or more. In 1 case (a patient with hemophilia) the corpuscles settled so much before coagulation that they made up but one-quarter of the bulk of the blood. In this case the coagulation time was more than eight times normal. In another case of hemophilia the corpuscles settled to about one-half the bulk, as shown in the accompanying illustration (Fig. 2).

The colorless clot above the corpuscles is evidently produced by the differences in specific gravity of the blood elements, and is the so-called "buffy-coat" described by Davy¹⁹ and Dalton²⁰ in

¹⁹ Researches, 1839, ii, 46.

²⁰ Treatise on Human Physiology, 1859, p. 195.

the first half of the last century. There were 47 cases with delayed coagulation time. Only 12 showed no settling of the corpuscles, and they were no longer than ten minutes at the most. A few of the 12 gave a clot of flimsy texture. As a rule therefore the delay in coagulation time goes hand-in-hand with the settling of the corpuscles and "buffycoat," and the two may almost be used as a check on each other. If either one or other is present the blood tested is not normal, but the usual combination of the two is conclusive.

Retraction of the Clot. There were but three cases in which no retraction of the clot took place. These were a fatal case of purpura hæmorrhagica, tested twice, a case of pernicious anemia, and a fatal case of jaundice and cholemia of unknown etiology.

Relation of the Coagulation Time to the Retraction of the Clot. The coagulation time in these three cases was twelve and one-half minutes, thirteen and one-half minutes, and seven minutes respectively. The various other cases with a delayed coagulation time showed a normal retraction of the clot, consequently the retraction of the clot did not seem to depend upon the mere delay in the coagulation time.

Relation of the Number of Blood Platelets to the Retraction of the Clot and to the Coagulation Time. The blood platelets were almost entirely absent in the case of purpura hæmorrhagica, as has already been pointed out by Denys,²¹ Hayem,²² and Duke.²³ The blood platelet count in the case of pernicious anemia was 1000. There was no examination of the blood platelets in the third case. Other cases with considerably decreased platelet counts showed fairly consistently delay in clot retraction. On the other hand, one case of hemophilia had a blood platelet count of 200,000, and retraction was normal. The problem of the relation of the blood platelets to the retraction of the clot is now being studied further, but in general these cases tend to suggest that the blood platelets have more to do with the retraction of the clot than with its actual formation, as has already been pointed out by Duke.²⁴

The color abnormalities observed have been chiefly three: The lighter color of the blood in severe anemias, the chocolate-brown color in leukemia, and the definitely yellow serum expressed from the retracting clot in cases of jaundice and pernicious anemia.

SUMMARY. A simple method of determining the coagulation time of blood has been studied. It obviates the contact of blood with tissue juice which introduces a larger element of error. The method seems reliable in ordinary room temperatures. In cases tested the tendency to bleed corresponded closely to the coagulation time.

²¹ La Cellule, 1887, vol. iii: 1889, v, 189.

²² Presse Méd., 1895, p. 233.

²³ Arch. Int. Med., November 15, 1912.

²⁴ Loc. cit.

THE VALUE OF MASSAGE IN THE TREATMENT OF VARIOUS DISORDERS IN CHILDREN.

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THE purpose of this paper is to call attention to the value of massage in the treatment of malnutrition, rickets, and various other disorders in children. In adults we have recourse to this form of treatment in affections of the heart; in conditions of malnutrition, with flabby muscles, as in the various types of anemia; in convalescence from acute diseases, operations, or parturition; in the treatment of sprains and fractures; in affections of the joints, muscles, and nerves; and in constipation. In children, however, this valuable therapeutic measure has been largely neglected, and yet the results obtained in the majority of cases are better than in the adult. The operator must not only be patient and skilful, but should also have had considerable experience in the nursing care of children. The latter I have found exceedingly important, and I have been fortunate in having had for this work a trained nurse who had several years' experience in the nursing of children before taking up the study of massage.

Many observers have noted the fact that babies in hospitals, but especially in foundling asylums, do not thrive as well after they have reached a certain period in convalescence from acute illness as they do under less favorable circumstances in their own homes. The reason for this is not difficult to determine. In the majority of hospitals the baby is left in the cot all day, often with the bedclothes tucked in so snugly that the movements of the arms and legs are greatly impeded, the respiration and circulation are sluggish, so that he will not thrive so well as if he were picked up at the times of nursing and allowed to move his arms and legs more freely. In some hospitals this "mothering" of babies is considered an essential part of treatment, but usually the inadequate number of nurses prevents it being properly carried out. For babies convalescing from illness in hospitals or homes, or cases of malnutrition, massage is of great value, and excellent results have been reported by MacPhail.

Massage mechanically excites the vessels to action, hastening the circulation and emptying the lymph vessels. Thus the nourishment of the muscle cells is improved by forcing out the waste products and keeping them bathed in a constantly renewed stream of arterial blood. The rate of the heart beat and respiration are slightly accelerated. In fact all the bodily functions are stimulated to increased activity.

The question might well be asked: "Do children not object to

this form of treatment?" This depends largely upon the personality of the masseuse, but in my experience, after the first treatment, the child seems to enjoy the manipulation.

The duration of the treatment should not be more than twenty or thirty minutes, and during the first two weeks should be given daily. Subsequent to this three times a week is sufficient.

It is in cases of malnutrition, with loss of appetite, weak flabby muscles, and distinct pallor that the best results are noted. This is best illustrated by the following case.

M.M., aged twenty-two months, came under observation in July, 1910, and at that time weighed thirteen pounds and eleven ounces. She has been nursed until six months old, and was then given modified milk. At one year she weighed twenty-one pounds. During the next five months her weight remained about the same; her diet consisted of milk, orange juice, cereal, soft egg, broth, and junket, and she showed some growing disinclination to eat. Dentition was normal, and at fourteen months she began to walk. From the seventeenth to the twenty-second month the appetite grew less until she took less than ten ounces of food in twenty-four hours. Her physician made various changes in her diet without any benefit. During the last two weeks before I saw her she had been fed on oatmeal water, but of this she took only a small quantity. As soon as food was offered to her she would "gag" and attempt to vomit. Her face became drawn so that she looked like a withered old woman; she was pale and emaciated and muscles flabby, and there was some edema of feet and hands. The case was considered to be one of anorexia nervosa. During the first six weeks feeding with a catheter was resorted to, using a formula of three parts milk and one part water, and during that time she gained steadily, weighing fifteen pounds and two ounces. She then began to take her milk herself, and by November 10 weighed nineteen pounds and four ounces. She then contracted a severe bronchitis, with high temperature, and gradually lost weight until December 5, when she weighed sixteen pounds and twelve ounces. She took her food poorly, and there was considerable undigested fat in the stools, so that the percentage of fat in her milk was reduced to 2. During the next five weeks there was no gain in weight; her muscles became more flabby, and on January 10, 1912, without changing her diet in any way, massage was started. She at once showed improvement, so that at the end of one month she weighed nineteen pounds and thirteen ounces, a gain of three pounds and one ounce. During the next month she gained four pounds, her muscles became firm, she lost her irritability, and from that time on she thrived, so that now at four years she weighs forty-one pounds.

In another patient, aged ten months, in whom the weight had been stationary for two months, the muscles flabby, and an anemia

present, so that the red blood corpuscles numbered 3,900,000 and hemoglobin 60 per cent., massage was started without making any change in diet. During the first month there was an increase in weight from sixteen pounds and two ounces, to eighteen pounds and twelve ounces, and at one year she weighed twenty pounds and twelve ounces. The red corpuscles at that time numbered 4,850,000, and the hemoglobin was 90 per cent. The most noticeable thing in this case was the increase in the amount of food taken within three days after massage was started.

Great benefit is obtained in the treatment of rickets from massage. In these cases the muscles are flabby, the circulation is sluggish, and the extremities emaciated. Because of the weakened condition the child takes no exercise, and with massage properly given the muscles become firm, the circulation is improved, and the extremities become stronger, so that the child itself will take more exercise. Furthermore, many of the deformities, such as bowing of the legs, can be prevented or corrected.

By massage combined with other exercises I have also seen complete correction of the deformity due to scoliosis before there was little or any change in the vertebræ.

In poliomyelitis after the acute stage has passed, massage has been used with such marked benefit that it is now looked upon as the most important therapeutic measure available for the treatment of the paralyzed muscles. I should like to call attention to its use in the prevention of the spastic contractures in cases of polioencephalitis or other conditions in which there is upper neurone destruction. The following case illustrates this very well:

K. B., aged five years and nine months, first came under observation in September, 1908. At that time, when she was eighteen months old, she had a severe attack of polioencephalitis, with right-sided convulsive twitchings, which kept up for twelve hours, and a temperature of 104° . The next day she had complete hemiplegia of the right side, with aphasia. During the next four days the temperature gradually returned to normal, but the aphasia and hemiplegia persisted. At the end of two weeks, as soon as the sensitiveness of the right arm and leg would permit, massage was started, and has since been continued every morning until the present time, by the mother, who after the first two weeks of treatment learned to give it herself. There was steady improvement, so that at the end of four months she could walk, and there has never been any evidence of spasticity in the right arm and leg. At the present time, with the exception of some of the finer movements of the fingers, she can use the right arm as well as the left, and both the right arm and right leg measure a trifle more than the left.

For a long time massage has been regarded as a useful therapeutic agent in constipation in adults, but seldom do physicians

resort to it in children. From a thorough trial I am convinced that it is just as useful in children as it is in adults.

Another group of cases in which massage is useful is in nervous children. Much can be accomplished by putting them to bed, carefully supervising the diet, and resorting to massage to keep up the nutrition. It is astonishing to see the improvement in a period of two weeks.

In cardiac lesions in children the result of acute rheumatism, the necessity of keeping these cases at rest for many weeks and months, in order to allow the heart muscle to regain its tone, is imperative. These patients will get up much stronger if after the febrile period has passed they are given massage, with first passive and then resisted movements.

Many other conditions might be mentioned where massage is useful, but in general the indications for its use are the same as in the adult, and the results are equally as good.

SOME HEMATOLOGICAL FINDINGS IN PELLAGRA.¹

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INTRODUCTION. The material upon which the following report is based was obtained from cases of pellagra which were sent from the field headquarters of the Commission at Spartanburg, South Carolina, together with slide specimens of pellagrous blood taken from cases in South Carolina and forwarded for study to the New York Post-Graduate Medical School and Hospital during the summer and early fall months of 1912. In spite of the fact that the number of cases under consideration at that time was not large, nevertheless, it seemed advisable to record briefly the most important points in connection with the work that had already been done.

The blood was examined with a view of determining the hemoglobin content, the number of red and white cells per cubic millimeter, the differential leukocyte count, and at the same time the general morphologic characteristics of the blood in stained preparations. A few observations were also made on the coagulation time.

A review of the literature on this particular phase of the hematology of pellagra reveals an agreement of opinion in regard to the presence of a mild degree of secondary anemia of the chlorotic type

¹ This is the first of a series of reports of work performed under the auspices of the Thompson-McFadden Pellagra Commission of the Division of Tropical Medicine, Department of Laboratories, New York Post-Graduate Medical School and Hospital, ultimately to be issued as a complete volume by the Commission.

without any marked structural or tinctorial alterations in the red corpuscles unless the anemia is pronounced. The majority of investigators state that the total leukocyte count varies, and that occasionally a leukocytosis exists which in most instances cannot be accounted for by the presence of a definite complication. The differential leukocyte count has apparently proved to be the most interesting and variable feature, and, judging from the available data, a fairly constant departure from the normal seems to be found in a large number of cases. Lavinder, in 1909, found "a relative large mononuclear increase with an absence of eosinophilia, except in cases with such complications as roundworms or hookworms." Sambon, working in Italy, also noticed a relative increase of the large mononuclear leukocytes. Contrary to these findings, Buhlig at the Peoria State Hospital, failed to demonstrate any increase in the large mononuclears. Bardin, quoted by Niles, found in uncomplicated cases of pellagra a lymphocytosis, with a corresponding reduction in polynuclears and a marked reduction in eosinophiles. Lavinder states that Fiorini, Gavini, and Masini in Italy found a decided eosinophilia. In the recent work of the Illinois Pellagra Commission no significant changes were observed in the differential leukocyte count.

TECHNIQUE EMPLOYED. The blood was taken for examination in the midforenoon or midafternoon. The percentage of hemoglobin was estimated with the Sahli hemoglobinometer, two "readings" being made and the results averaged; this method was found quite satisfactory. The erythrocytes were counted with a Thomas-Zeiss apparatus, using a dilution of 1 to 200 and counting the corpuscles on the four corner "blocks" of twenty-five small squares in two drops. The average was then taken and the number of cells per cubic millimeter computed on this basis. In estimating the number of leukocytes a Zappert-Ewing chamber was used, thus affording an opportunity of counting 9 square millimeters in one drop. Two such determinations were made from a dilution of 1 to 20 in a "Rieder" pipet and the average taken; the usual calculation was then made. A difference of not more than twenty cells per field (high power) in the red count and eight cells per field (1 square millimeter, low power) in the white count was permissible. If a greater discrepancy existed a third drop was usually sufficient to rectify it, in either count.

For differential leukocyte counting films were made on clean, new slides, and a preparation selected in every case, on which the distribution of the corpuscles was moderately thin. Five hundred cells were counted over the midportion of each slide, care being taken not to encroach too closely on the ends, where frequently there is a relative increase in the more bulky leukocytes. The blood was stained with Wright's modification of Leishman's polychrome eosin-methylene blue mixture. The following classification was

adopted: polynuclear neutrophiles, small lymphocytes, large lymphocytes, large mononuclears, transitionals, eosinophiles, and mast cells. Differentiation between the small and large lymphocytes was to a certain extent unsatisfactory, inasmuch as intermediate gradations in size were occasionally encountered. Mononuclear cells measuring 12 to 15 microns in diameter, and having a comparatively wide zone of protoplasm, were classified as large lymphocytes; these were generally found to contain round nuclei staining not quite so intensely as the nucleus of the small lymphocyte. The large mononuclear leukocyte was recognized by its size, being two to three times that of a red blood corpuscle and containing a pale oval nucleus, frequently eccentric in position; the protoplasm was usually abundant, and feebly basic. It was realized that distinction between these two cells is a matter of no little difficulty, and depends to a large extent upon the personal equation, which forms an important factor in this much-debated question in the cytology of the blood. The reason for attempting to classify these types separately arose from the desire to ascertain whether the so-called large mononuclear leukocyte exhibited any relative or absolute variation from normal limits.

The patients examined were divided into two groups, A and B. Under Group A were included those cases that were under observation in the hospital at the time the examinations were made. These patients received no medicine, and were allowed a liberal diet. In Group A the hemoglobin percentages were determined, the red and white cells counted, and differential leukocyte counts made; this series of investigations is designated as "complete blood counts." As will be seen in Table I, several such complete counts were made on most of the cases. Under Group B (Table II) are included those cases in which only differential leukocyte counts were done, it not being convenient to make a more detailed examination at the time.

ANALYSIS OF FINDINGS. In Table I the hemoglobin percentages show considerable variability, ranging from 58 to 107 per cent., with an average of 83 per cent. The erythrocytes are not markedly decreased, the lowest number being 3,920,000 per c. mm. As will be observed, several counts are 5,000,000 and over, the highest figure being 5,440,000. This occurred in the only male patient of the group, and was associated with a moderate reduction of the hemoglobin (65 per cent.). The patient was a poorly nourished individual, who was suffering from a mild attack of pellagra of about one year's duration. The majority of the members of this group appeared decidedly pale and anemic, according to general clinical criteria, and it was a matter of surprise to note the comparatively slight reduction in erythrocytes and hemoglobin that existed. The average red-cell count was 4,758,000 per c.mm.

TABLE I (GROUP A).—COMPLETE BLOOD COUNTS.

No.	Date.	Sex	Age.	Hemoglobin. Per cent.	Erythro- cytes. Per c.mm.	Color index.	Leuko- cytes.		Polynuclears.		Small lymphocytes.		Large lym- phocytes.		Large mono- nuclears.		Transi- tionals.		Eosino- philes.		Stage of disease and clinical remarks.	
							Per c.mm.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
1	1912	F.	36	70	5,290,000	0.6	6,300	49.60	3125	40.00	2520	3.00	189	3.40	214	0.60	38	3.00	189	0.40	First attack, severe; duration, three weeks; watery diarrhea; strongyloides intestinalis numerous in stool.	25
	June 4			85	5,430,000	0.7	7,000	52.80	3696	27.20	1904	6.20	434	2.60	182	1.60	112	8.00	560	1.60		
	June 15			85	5,200,000	0.8	7,400	43.60	3227	40.00	2960	10.70	740	1.20	89	1.00	103	3.40	251	0.40		
	June 24			83	5,140,000	0.8	9,000	59.30	5337	24.60	2214	8.70	783	2.80	180	0.70	63	3.70	333	1.00		
	July 1			83	5,060,000	0.8	9,100	47.40	4313	42.00	3822	2.80	255	2.80	255	2.00	182	2.40	218	0.60		
2	June 4	F.	17	60	4,620,000	0.7	8,300	71.00	5893	18.00	1494	2.20	183	3.00	249	2.20	182	3.00	249	0.60	Recurrent attack, severe; duration, three weeks.	35
	June 14			84	4,640,000	0.9	8,800	50.40	4435	33.40	2940	5.80	510	1.80	158	4.20	370	4.00	353	0.40		
3	July 1	M.	60	87	4,700,000	1.0	8,200	63.40	5199	21.20	1738	5.40	443	4.20	295	1.40	115	4.40	361	0.60	First attack, mild; duration, one year.	26
	June 12			98	5,440,000	0.6	6,500	66.60	4329	35.00	1560	1.40	91	4.20	273	2.00	130	1.40	91	0.40		
4	June 19	F.	40	93	5,040,000	1.0	7,100	55.80	3962	24.00	2485	6.75	540	2.00	160	1.00	99	1.60	114	0.20	Recurrent attack, mild; duration, two and one-half months.	29
	June 25			95	4,900,000	0.9	8,000	55.00	4400	31.00	2480	6.75	540	2.00	160	1.00	99	1.60	114	0.20		
5	July 0	F.	32	105	4,000,000	1.3	7,200	62.00	4404	27.40	1972	4.80	346	2.00	144	0.80	58	2.60	187	0.40	Recurrent attack, severe; duration, two months.	10
	July 10			100	4,560,000	1.0	7,200	55.00	3960	33.00	2376	8.20	159	4.20	303	1.60	115	3.60	259	0.50		
6	July 16	F.	18	102	4,200,000	1.1	10,000	45.60	4550	39.00	3900	8.20	820	5.50	550	1.30	130	1.40	140	0.10	First attack, mild; duration one month; no intestinal parasites found in stools.	28
	July 27			107	4,400,000	1.2	11,000	56.50	6215	28.00	3080	6.50	715	3.20	256	0.40	32	4.40	332	0.20		
7	Aug. 8	F.	20	86	4,800,000	0.9	9,000	69.00	6210	21.60	1944	4.40	396	1.80	162	1.40	126	1.80	162	0.20	First attack, mild; duration, two weeks.	48
	Aug. 17			81	4,800,000	0.8	14,000	60.20	8420	21.40	2096	5.60	784	3.40	476	1.40	196	7.80	1092	0.40		
8	Aug. 7	F.	36	100	4,500,000	1.1	12,000	71.20	8544	15.00	1700	5.40	648	5.60	672	0.60	54	5.40	486	0.20	Recurrent attack, mild; duration, 3 weeks.	58
	Aug. 8			90	5,000,000	0.9	16,800	76.40	12353	16.20	2721	1.20	202	3.00	504	1.00	100	2.00	336	0.40		
9	Aug. 8	F.	28	78	4,800,000	0.8	14,000	78.60	6000	32.00	3220	3.00	300	1.00	100	1.00	202	3.00	300	0.40	First attack, severe; duration, 3 mos.	82
	Aug. 17			67	5,000,000	0.6	14,000	68.25	7288	22.50	2477	1.80	259	0.80	115	4.50	495	2.50	275	0.75		
10	Sept. 7	F.	43	58	4,410,000	0.6	11,000	66.25	7128	17.20	2475	1.80	275	1.00	110	4.50	495	2.50	275	0.60	Recurrent pulmonary tuberculosis.	65
	Sept. 17			85	3,920,000	1.0	16,000	61.80	10358	32.00	5312	2.80	465	1.60	222	0.20	222	2.00	216	0.60		
11	Sept. 17	F.	34	65	5,400,000	0.6	18,000	72.60	13068	18.00	3348	3.20	576	1.80	180	2.40	432	2.40	396	0.40	Recurrent attack, mild; duration, five months.	01
	Sept. 24			100	4,380,000	1.1	9,100	61.30	5578	31.50	2866	3.50	319	1.30	118	1.50	109	0.90	396	0.40		
12	Sept. 28	F.	33	83	4,140,000	1.1	12,700	64.20	8143	26.40	3553	4.00	508	2.00	254	1.20	152	1.80	229	0.40	Recurrent attack, mild; duration, four months.	31
	Average																					

* The term "severe" implies the presence of gastro-intestinal symptoms, nervous manifestations, and extensive skin lesions.
 † Two hundred and twenty leukocytes counted.

TABLE II (GROUP B).—DIFFERENTIAL LEUKOCYTE COUNTS ONLY.

No.	Sex.	Age.	Polynuclears.	Small lymphocytes.	Large lymphocytes.	Large mononuclears.	Transitionals.	Eosinophiles.	Mast cells.	Stage of disease and clinical remarks.
1	M.	23	52.80	34.40	1.20	1.60	1.00	9.00	Recurrent attack, severe; duration, one month; stools not examined.
2	F.	34	59.20	32.00	2.40	2.40	2.00	2.00	First attack, severe; duration, one month.
3	F.	30	56.00	32.00	3.40	1.00	0.40	7.20	Recurrent attack, mild; duration, two months; stools not examined.
4	F.	19	56.00	33.40	1.80	2.00	1.80	5.00	First attack, mild; duration, one month; no intestinal parasites found in stools.
5	F.	40	66.00	28.00	4.00	1.00	0.60	1.00	0.20	First attack, mild; duration, two months.
6	F.	35	69.80	23.60	2.20	2.40	0.60	1.20	1.40	Recurrent attack, mild; duration, one month.
7	F.	26	49.20	39.00	4.00	1.40	1.60	3.40	0.20	First attack, severe; duration, one month.
8	F.	21	50.00	40.20	4.20	2.60	1.20	0.80	First attack, severe; duration, two months.
9	F.	30	60.60	32.80	2.80	2.60	0.40	2.40	0.40	Recurrent attack, mild; duration, four months.
10	F.	38	58.40	31.60	4.00	1.60	2.00	4.00	Recurrent attack, mild; duration, two months.
11	F.	38	56.80	31.60	2.40	2.80	2.40	3.20	First attack, mild; duration, two months.
12	F.	30	51.20	36.40	4.40	2.40	1.00	0.60	Recurrent attack, mild; duration, two months.
13	F.	35	61.00	30.60	4.20	2.40	1.20	1.80	1.60	Recurrent attack, mild; duration, five months; recovering.
14	F.	36	56.40	35.00	4.20	1.40	0.40	2.80	1.00	Recurrent attack, mild; duration, one month.
15	F.	27	34.80	50.40	5.20	4.80	0.40	5.60	1.00	First attack, mild; duration, three months; recovering.
16	F.	44	37.80	40.40	10.00	4.80	0.40	2.60	1.00	Recurrent attack, mild; duration, four months; recovering; no intestinal parasites found in stools.
17	F.	32	47.60	40.40	5.20	1.20	0.40	7.80	Recurrent attack, mild; duration, four months; recovering.
18	F.	36	62.60	26.00	3.00	0.20	1.00	3.80	1.00	Recurrent attack, severe; duration, five months; recovering.
19	F.	28	68.00	21.80	3.40	2.00	1.00	3.00	1.00	Recurrent attack, mild; duration, three months; recovering.
20	M.	25	62.00	27.00	6.00	1.50	5.00	1.00	First attack, mild; duration, one month.
21	M.	36	57.00	31.00	5.00	0.50	0.20	2.00	0.80	Recurrent attack, mild; duration, three months; recovering.
22	M.	34	50.00	33.00	8.00	5.00	1.00	First attack, severe; duration, two months.
23	F.	19	55.00	38.00	4.00	1.00	1.00	Recurrent attack, severe; duration, four months; recovering.
24	M.	35	50.00	41.00	5.00	3.00	0.80	4.00	0.40	First attack, mild; duration, four months.
25	F.	32	64.00	23.00	7.00	1.00	2.00	Recurrent attack, mild; duration, three months.
26	F.	26	56.00	32.00	8.00	2.00	1.00	1.00	First attack, severe; duration, two months.
27	F.	40	60.00	30.00	7.00	1.00	0.60	3.00	Recurrent attack, severe; duration, five months; stools not examined.
28	M.	22	54.00	38.00	6.00	1.20	3.00	Recurrent attack, mild; duration, four months; recovering.
29	F.	48	63.00	25.00	5.20	3.00	2.00	0.50	First attack, mild; duration, two months.
30	M.	39	54.60	32.40	6.00	3.00	0.50	1.00	First attack, severe; duration, four months.
31	F.	40	58.00	30.00	6.00	3.00	1.00	2.00	0.50	First attack, mild; duration, two months.
32	F.	34	60.00	27.00	8.00	3.00	0.50	3.00	First attack, severe; duration, four months.
33	F.	17	37.50	44.00	10.00	1.00	1.00	1.20	First attack, severe; duration, one month.
34	F.	38	73.60	20.00	3.20	2.00	1.00	3.00	0.40	First attack, severe; duration, three months; recovering.
35	F.	22	58.20	28.60	7.20	2.00	1.00	2.20	First attack, severe; duration, three months; recovering.
36	F.	58	60.20	26.20	9.40	2.00	1.00	0.60	First attack, severe; duration, three months; recovering.
37	M.	8	54.40	32.00	9.60	2.00	1.00	0.60	0.26	First attack, severe; duration, three months; recovering.
Average			56.00	32.37	5.28	1.98	0.87	2.94	0.26	

* The term "recovering" means that the patient had no active signs or symptoms of pellagra when the blood was examined.

The color index was 1 or 1 plus in twelve determinations, the highest index being 1.3. In twenty instances it was under 1, the lowest being 0.6; the average index was 0.8. A careful examination of the stained blood films exhibited practically no changes in size, shape, or coloring of the red cells; nucleated corpuscles were never seen nor were there any staining variations from the normal, such as polychromatophilia and basophilic granulation. The average leukocyte count was 10,403 per c.mm., a trifle above the maximum normal. A slight or moderate leukocytosis existed in severe cases at some time during their residence in the hospital. No complications could be discovered in these patients. One patient with chronic pulmonary tuberculosis and much emaciation had a leukocytosis of 11,000 to 14,000; she had an irregular temperature, not exceeding 100.2° F. All the other cases were afebrile, and frequently had subnormal temperatures.

The differential leukocyte count revealed an absolute polynucleosis in those cases associated with a leukocytosis of over 10,000, except in one instance. Three of these cases, however, showed a slight relative decrease in the polynuclears. Out of thirty-two differential counts in this group, twenty-four gave a relative and, in addition, an absolute lymphocytosis, including under this term both small and large forms of lymphocytes. The average total lymphocytosis of the series was 33.99 per cent. The average large mononuclear count was 2.59 per cent. The highest percentage recorded was 5.5 per cent. The transitional forms average 1.5 per cent. These last two types taken together (Ehrlich's classification) form 1 to 6 per cent. of the leukocytes in normal blood; therefore, from the above figures it cannot be said that they show any constant alteration from the normal. The average eosinophile count of 2.73 per cent. is within normal limits. A few cases showed slight eosinophilia, the highest being 8 per cent. in which patient *strongyloides intestinalis* were found in the stools.

The coagulation time was determined in the first three cases with a Brodie-Russell coagulometer and was found to be six minutes and twenty seconds, four minutes and eight seconds, four minutes and twenty-five seconds, respectively, all of which readings are within the normal range for this instrument.

Table II. The differential leukocyte count on a series of slides taken from 37 cases at their homes in South Carolina was carefully determined without discovering any essential variation from the average results obtained in Group A. The average lymphocytosis of 37.65 per cent. is a little higher than in the previous group.

SUMMARY. From a consideration of the above data it is evident that there occasionally exists in pellagra a variable degree of chlor-anemia, which, however, is not a prominent feature of the attack. The disease, apparently, may be present for some time without leading to any anemic changes. Whether the anemia is due to the actual

existence of pellagra, or is the result of an indefinite train of antecedent conditions extending over a period of time before the inception of the disease, is difficult to say. On the other hand, many cases are perfectly well up to the onset of the attack.

One of the most noteworthy features in connection with the leukocytes is the not infrequent presence of a leukocytosis, which appears to be inexplicable in the light of our present knowledge of the disease. This might suggest the possibility of an infectious etiology of obscure origin, or may be due to complicating disturbances. The lymphocytosis is interesting and is probably in accordance with the general cachectic condition of most pellagrins who are also often the subjects of gastro-intestinal disorders.

This investigation would seem to indicate that there are no characteristic or constant variations in the large mononuclear leukocytes and eosinophiles.

The writer wishes to thank Drs. P. S. Barrett, R. M. Brown, S. S. Irwin, and E. Kister, of the resident hospital staff, for assistance in making the blood examinations.

COMPLETE HEART-BLOCK, WITH RAPID IRREGULAR VENTRICULAR ACTIVITY.

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THE following case of heart-block presents unique and unusual features which warrant its report:

History. L. W., aged twenty years; born in the United States; the oldest of three children; entered the surgical wards of the German Hospital February 20, 1912.¹ His family history presents nothing abnormal. He had an attack of scarlet fever and diphtheria about five years ago, from which he recovered entirely. Except for two mild attacks of gonorrhea, the last one occurring one year ago, he had been absolutely well until six months before admission. At that time he began to complain of indefinite abdominal symptoms. He had constipation, nausea, anorexia, and general abdominal pains, usually more marked on the right side; fever and night sweats. He lost about forty pounds in weight. There was occasionally a dry cough, but no expectoration. For two years he had been in the habit of counting his pulse, and he says that until his present illness it had always been between 70 and 80.

¹ I am indebted to Dr. Willy Meyer and Dr. M. Rehling, Attending and Adjunct Surgeons to the German Hospital, New York, for permission to study and report this case.

Physical Examination. On the left side of the neck, partly beneath the sternomastoid muscle, there was a single gland about the size of a walnut, movable and somewhat tender. The gland had been enlarged several months. It did not resemble the ordinary tuberculous glands of the neck. The von Pirquet test was positive, and the Wassermann reaction negative. The urine was normal. The blood pressure usually ranged about 120 mm. Hg. systolic and 105 diastolic. Before operation the rectal temperature ranged from 101° to 103°.



FIG. 1.—X-ray of chest, showing advanced shadows about root of the lungs, particularly on the left side.

Lungs: Many examinations of the lungs showed no abnormal physical signs; no rales; no areas of dulness; no signs of tuberculous infiltration. Röntgenograms of the chest (Fig. 1), on the other hand, showed abnormal shadows about the root of the lungs, particularly on the right side. These infiltrated areas were apparently deep-seated, and this fact probably accounted for the lack of abnormal physical signs. The pictures also showed infiltrating areas in the upper lobe of the left lung.

Heart: The apex beat was forcible, somewhat diffuse, situated in the fifth intercostal space, 8.5 cm. from the middle of the sternum, and just within the nipple line. The right border of cardiac dullness was about 1 cm. from the right sternal border. Orthodiascopic examination also showed the heart borders to be normal in size and form. There was a soft systolic murmur accompanying the beginning of the first sound at the apex and a marked roughening of the first aortic sound. At the root of the neck there was a frequent vigorous jugular pulsation. The radial pulse was regular, except for occasional shorter beats, and often so dicrotic as to give the impression that a premature contraction (extrasystole) had occurred. The apex impulses represented beats, all of which were transmitted to the wrist. Upon admission to the hospital his pulse was 50. During his stay and after his discharge from the hospital his pulse was usually 48 to 54; it was occasionally 42, and sometimes 70. Though weak and febrile the patient was able to walk fairly well. There was no dyspnea; no dizziness; no edema of the ankles; no evidence of decompensation.

His abdomen was tense; ascites was present; irregular doughy masses were felt in both hypochondria. A diagnosis of tubercular peritonitis was made.

Laparotomy was performed by Dr. Willy Meyer March 9, 1912. About a pint of sanguineous peritoneal fluid escaped. The cecum was indurated and studded with tubercles. There were many hard and large nodes in the mesentery; a piece of one of them was removed for microscopic examination; this showed "numerous isolated tubercles of typical structure, consisting of caseous centres of various sizes, surrounded by layers of epithelioid cells, among which are found numerous Langerhans giant cells."² No radical operation was attempted. The postoperative course was disturbed by a femoral thrombosis lasting two weeks. After operation the temperature gradually fell, so that when the patient left the hospital it ranged between 100° and 101°. Since then (May 21, 1912) his rectal temperature has not been over 100°. He has felt stronger, but occasionally has complained of slight abdominal pains. He has gained twelve pounds in weight. At the last examination (May 31, 1912), except for a slight soft impurity of the first sound at the apex, the heart sounds were normal. Tracings taken in February, 1913, showed that complete heart-block was still present.

During the patient's stay in the hospital, polygraphic tracings were made almost daily, twice before and after the administration of atropine. Many tracings have been taken since, and on two occasions electrocardiographic curves were obtained during the administration of atropine. Digitalis has not been given at any time.

² Report from the Pathologic Department of the German Hospital.

Polygraphic Tracings. Tracings showing complete *A-V* dissociation are reproduced in Fig. 2. Instead of the normal succession of *a-c-v* waves corresponding to the normal sequence of the cardiac cycle, there is absolute independence of the auricular and ventricular contractions. The auricular beats (*a* waves) occur at regular intervals, but have no fixed sequential relation with the ventricular beats (*c* waves). The *a* waves precede, coincide with, or succeed the *c* waves. Radial tracings (Fig. 3) taken during the operation also suggest that complete heart-block was present at that time, as the rate and arrhythmia were the same as when complete heart-block is known to have existed. The tracings also show alternation (*R, R'*, Fig. 3).

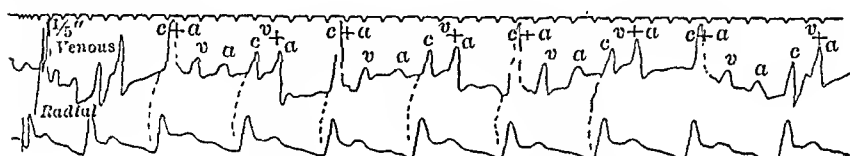


FIG. 2.—Complete block; marked diastolic notch in radial.



FIG. 3.—Radial pulse during operation.

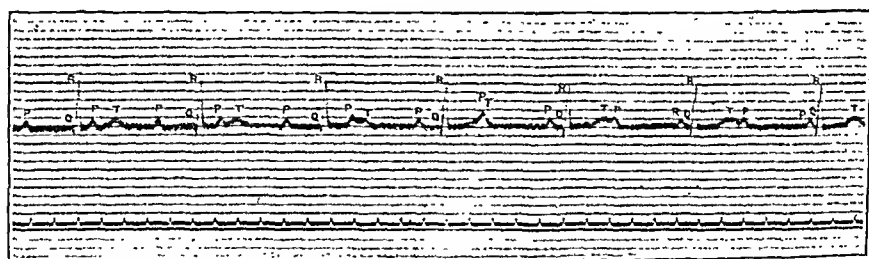


FIG. 4.—Complete dissociation.

*Electrocardiographic Curves.*³ Electrocardiograms (leads 1, 2, 3) were taken before atropine was injected. During the period of atropine poisoning only the second lead was taken. The galvanometric curves (Fig. 4) just as did the polygraphic tracings, showed complete dissociation. Sometimes the *P-R* interval (corresponding to the *As-Vs* interval) was small, sometimes large, and occasionally the *P* and *R* coincided. At times the *P* and *T* waves fell together, producing summation waves of different sizes.

³ I am indebted to the Cardiographic Department of the Rockefeller Hospital for taking these curves and for cooperation in the study of this case.

Discussion of the Polygraphic and Electrocardiographic Curves. The usual ventricular rate in complete heart-block is between 25 and 35. Rates of 60 have been described by Windle,⁴ but they are rare. In the case of heart-block reported by Hay⁵ and later by Hay and Moore,⁶ when the ventricular rate was 80, the block was relieved and the auricles and ventricles beat coördinately. In heart-block and auricular fibrillation incident to digitalis poisoning a rate of 70 has been reported by Mackenzie⁷ and one of 90 by Lewis.⁸ In incomplete heart-block associated with auricular tachycardia the ventricles also beat rapidly. Such cases were first reported by Herts and Goodhart,⁹ Rihl,¹⁰ Cohn,¹¹ and Lewis.¹² During the first atropine administration in the case now reported the ventricular rate was also unusually high, varying from 54 to 77, while the auricular rate ranged from 108 to 124. The auricular and ventricular rates in the second atropine test varied respectively between 95 and 115 and between 50 and 69. During these periods the ventricular contractions were irregular. This irregularity was occasionally felt by palpating the pulse, and was also seen in the polygraphic tracings when atropine had not been given. An arrhythmia of this type is often the result of premature contractions originating at some point other than that in which the rhythmic ventricular beats are being generated. The aberrant origin of such beats is detected by the difference in shape of the electrocardiographic complexes between the usual and unusual beats. The shape of the electric complexes of all the beats in this case, however, was identical, indicating that they had a common origin. After the administration of atropine the interventricular interval ($R-R$) was for the most part fairly uniform, being about one second; shorter intervals varied from 0.686 second to 0.851 second. It was found in the shorter beats that the time between the R waves and P waves immediately preceding them was in every instance but one between 0.1 and 0.2 second (Table I): that is to say, the $P-R$ time in these cycles fell within normal limits. Taken by themselves it would appear that these shortened ventricular intervals resulted from contractions stimulated by the preceding auricular contractions. As they occurred after the administration of atropine the conclusion seemed warranted that the degree of heart-block had been decreased by the removal of the depressing influence of the vagus nerves on conduction, and that occasionally

⁴ Heart, i, 2.

⁵ Lancet, January 20, 1906.

⁶ Ibid., November 10, 1906.

⁷ British Med. Jour., 1911, ii, 872.

⁸ Heart, iii, 284.

⁹ Quart. Jour. Med., 1908-1909, ii, 213.

¹⁰ Zeitschr. f. exp. Path. u. Therap., 1911, ix, 277.

¹¹ Jour. Exper. Med., 1912, xv, i, 50.

¹² Heart, iii, 299.

stimuli generated by auricular contractions were able to pass over the conducting system and to originate ventricular contractions. These stimuli reached the ventricles before their time for rhythmic contraction and apparently resulted in sequential heart-beats. In the second test made at a later date the short ventricular cycles also appeared, but the relation between the *P* and *R* waves already described did not recur. It appears therefore that short ventricular beats can occur, that ventricular arrhythmia results, and that the arrhythmia may be independent of impulses descending from the auricle. The origin of the shorter beats in the first experiment may have been accidental. No positive conclusion was drawn as to the degree of block that was present. The occasional presence of 2 to 1 heart-block (Fig. 5, Table II) is only apparent, and is due to the ventricular rate being at times one-half of the auricular. Continuations of such tracings soon show complete block when the auricular or ventricular rates begin to vary. The

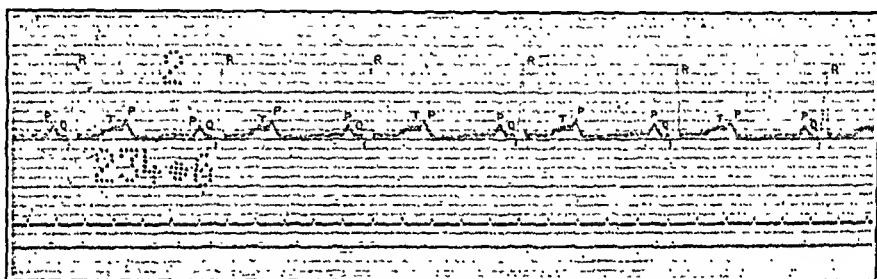


Fig. 5.—Apparent 2 to 1 block in this portion of the tracing.

atropine had a marked effect in increasing the ventricular and auricular rates in the first administration and a less marked effect on the ventricular rate in the second. On this occasion measurement of the curves showed a peculiar auricular rhythm; there were alternate short and long interauricular (*P-P*) intervals (Table II).

The cause of heart-block in this case is difficult to determine. A syphilitic lesion involving the *A-V* bundle can be excluded because of the absence of any syphilitic manifestations and of a positive Wassermann reaction. The patient never had rheumatism, and so inflammatory infiltration of the conduction system is likewise excluded. The favorable progress of the patient makes it seem unlikely that a neoplasm involved the atrioventricular bundle. The history suggests a direct connection between the onset of tuberculous peritonitis and of heart-block. The Röntgenograms show abnormal shadows at the pulmonary hilus, representing enlarged lymph nodes. The nodes are probably tuberculous. An extension of the tuberculous process to the heart is possible. A few cases of solitary tubercles in the heart have been published.

In one Tabora and Tilp¹³ describe a pulse rate of 48. There is no reason to believe that diffuse tuberculous myocarditis is present in this case, but the suspicion that a solitary tubercle is pressing upon or destroying the *A-V* bundle cannot be dismissed.

The radiographic shadows in question may represent mediastinal nodes, and it may be that these exert pressure on the deep cardiac plexus and its branches. This plexus, consisting of branches from the vagus and sympathetic and sending filaments to the heart, is located over the bifurcation of the pulmonary artery, posterior to the arch of the aorta and anterior to the lower end of the trachea; the two distinct portions—right and left—are united around the lower end of the trachea. What effect such compression may have in causing heart-block cannot be stated.

Summary and Conclusions. A case of complete heart-block with rapid arrhythmic ventricular action is recorded. Atropine was administered upon two occasions. The first time the block was probably relieved; at the second it was not. The rate of both auricles and ventricle was increased. The electrical complexes of all the ventricular cycles, long and short, were identical. It is concluded therefore that ventricular arrhythmia not due to ectopic ventricular contractions may occur in heart-block, assuming the block to be complete. The cause of the block and the exact nature of the lesion has not been ascertained. It is supposed that a factor besides that due to the vagus nerves is involved in the production of block.

I wish to express my indebtedness to Dr. A. E. Cohn and Dr. G. C. Robinson for valuable assistance in the study and preparation of this case.

TABLE I.

Cycle	Q-Q Interval.	P-Q Interval.	P-P Interval.
3- 4	.965	.466	.516
4- 5	.750	.125	.508
5- 6	.988	.522	.600
6- 7	.784	.255*	.547
7- 8	.964	.063	.655
8- 9	.965	.495	.500
9-10	.712	.121	.533
10-11	.964	.539	.564
11-12	.988	.417	.547
12-13	.755	.104	.564
13-14	.971	.666	.564
14-15	.732	.158	.562
15-16	.966	.041	.625
16-17	.956	.400	.500
17-18	.686	.100	.545
18-19	.964	.500	.627

In all the tables the measurements are given in fractions of seconds.

¹³ Strassburger med. Zeit., 1908, Heft 3.

Shorter beats and normal P - Q intervals (between 0.1 and 0.2 seconds) are in heavy figures.

With one exception (marked *) P - Q intervals of short beats are normal.

TABLE II. CURVE, FIG. 5.

Cycle.	Q-Q Interval.	P-Q Interval.	P-P Interval.
1	1.190	.055	.600
2	1.193	.041	.600
3	1.160	.051	.566
4	1.175	.043	.600
5	1.150	.048	.566
6	1.148	.051	.606
7	1.176	.042	.575
8	1.166	.050	.600
9	1.175	.046	.575
10	1.188	.050	.600
11	1.181	.054	.537
12	1.178	.030	.602
13	1.200	.050	.588

Auricular about twice the ventricular rate; no short ventricular beats.

Auricular rhythm shows alternating long and short beats.

THE ACUTE EFFECTS OF CAISSON DISEASE OR AEROPATHY.¹

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OF all the occupational diseases which follow in the train of advancing civilization, together with development of arts, sciences, and industries, none is of greater interest, none more dramatic in its manifestations, than the oftentimes tragic effects of the illness to which men are liable who work in compressed air in diving, or in subaqueous construction of tunnels, jetties, foundations for bridges, etc.

A man in all the vigor of health and strength descends to his daily task in the river tunnel; enters the compressed air; works his regular shift of three or four hours; comes out through the air lock by the ordinary method of decompression; ascends to the street and starts for home, feeling perfectly well.

Fifteen minutes later, without the slightest warning, he is attacked with intense boring pains in his legs and abdomen; or,

¹ Paper read before Section IV, No. 5, of the XVth International Congress of Hygiene and Demography, September 24, 1912

he staggers and falls helpless to the ground, paralyzed from his waist down. Fortunately he is if efficient treatment be near at hand, and by recompression in the medical air lock, his pains vanish, his paralysis disappears, and on the morrow he returns to his work as usual.

The evolution of theories and devices to enable man to subsist for a time under water begins with the age of Aristotle and Alexander the Great, and constitutes a fascinating study; but the first authentic mention of caisson disease is due to Trieger, the French engineer, who first successfully operated a practical caisson in 1839.

The material for this paper is mainly drawn from the writer's own experience of two and one-half years as a member of the medical staff in attendance during the construction of the East River tunnels from New York to Long Island City, the largest single enterprise ever attempted under compressed air, in which more than 10,000 men were employed and 3,692 cases of illness were reported by the medical director, Dr. F. L. Kcays.

To designate the train of symptoms resulting from work in compressed air various terms have been used, for example, "caisson disease," "divers' palsy," "compressed-air illness or sickness," "bends," etc.

In an earlier paper I ventured to employ the term "aeropathy" as being more inclusive, and, for philological reasons, more widely available in all languages, and this term I shall employ hereafter in this paper.

ETIOLOGY. At the outset we will state our acceptance of the theory that gas emboli in the blood and body tissues are the direct cause of aeropathy symptoms, and a clear understanding of the etiology is essential to the correct interpretation of the Protean manifestations of this disease.

The animal experiments of Boyle, in 1670, laid the foundation for this theory, and its elaboration by Hoppe-Seyler, Bert, von Schrötter, Silberstern, Leonard Hill, and others has placed the gas emboli theory in an impregnable position.

Practically all autopsies if performed early upon victims of an acute attack of this disease show gas emboli in the veins and right heart.

All other theories may be dismissed at once upon the ground that none of them accounts for the formation of a single bubble of gas in the body fluids, an occurrence which we believe to be the one necessary factor in the etiology.

The fluids and tissues of a man working in compressed air become saturated with the gases of the atmosphere to a degree which depends upon (1) the amount of pressure (Dalton's law); (2) the length of exposure; (3) the vascularity and the absorptive ability of the individual tissue.

No symptoms ever develop while a man remains in the compressed air no matter what the degree of pressure nor length of exposure; hence we can state dogmatically that the disease is due solely to the ebullition of bubbles of gas (chiefly nitrogen) brought about by decompression, which is so rapid that the gases cannot be carried by the blood to the lungs and there gotten rid of gradually as they have entered; consequently they are set free as bubbles in the body tissues and fluids, with disastrous effects in many cases, forming emboli in the circulation or damaging tissues by the force of their expansion.

PHENOMENA OF COMPRESSION. Certain interesting phenomena are noted during the act of compression which are largely mechanical, and may be regarded as physiological; certainly they are in no sense symptoms of aeropathy.

1. The rising pressure forces inward the ear-drum membrane, causing discomfort, acute pain, or even rupturing this structure, unless the pressure be equalized by admitting air through the Eustachian tube, by Valsalva's method or an equivalent.

2. Slight rise in body temperature and sweating occur, due to the heat generated by the compression of the air.

3. The denser air offers a slight resistance to expiration and phonation. Whispering becomes impossible, and the lessened amplitude of vibration renders whistling difficult or impossible, and in such an attempt the non-vibrating lips give a sensation of slight numbness.

4. The voice loses its natural quality and sounds intensely nasal.

5. A sense of exhilaration and an ease of movement is experienced, and it is claimed that compressed-air work increases the appetite.

Other phenomena of compression have been reported, but are now generally discredited; thus,

Pallor of the skin and mucous membranes does not occur unless it be from nervousness on the part of the man entering compressed air for the first time.

There is no lessening of the volume of the pulse; no constant alteration in the blood pressure; no constant change in the rate either of the pulse or respirations.

The superficial veins do not collapse; the capillary circulation in a frog's foot continues unchanged. (Hill and others.)

There is no demonstrable change in the urinary or sweat excretion.

Hearing is not affected.

PHENOMENA OF DECOMPRESSION include chilling of the body, due to the falling temperature in the air lock, and one may at times note a crackling sound in the ears as the air escapes through the Eustachian tubes.

ONSET OF SYMPTOMS. The symptoms of aeropathy proper occur only as a result of decompression and after its completion.

The time of onset is from within fifteen minutes up to a few hours after decompression. Among the 3692 cases at the East River tunnels about 50 per cent. occurred within thirty minutes and 95 per cent. within three hours; however, 1 per cent. were delayed over six hours, and of these latter, four isolated and somewhat doubtful cases were said to have occurred between fifteen and twenty-three hours after decompression. (Keays.)

SYMPTOMS.—(1) *Pain* is by far the commonest symptom, occurring in over 88 per cent. of all cases, either as the only symptom or associated with others. Its most frequent (70 per cent.) site is in the lower extremities in the region of the knees, forcing the victim into an attitude which gives rise to the popular term “bends,” or “courbatures.” Next in frequency are pains in the upper extremities, about the elbows and shoulders in 30 per cent. Pains in the abdomen occurred in about 5 per cent. of the cases, but were of greater significance than were pains in the extremities in that they more often preceded or accompanied cases of severe prostration or paralysis.

2. *Vertigo*, or, in the parlance of the workers, “staggers,” was met with in over 5 per cent., and is explainable by the formation of bubbles in the labyrinth of the internal ear, or when accompanied by nausea and vomiting it may be due to cerebellar gas embolism.

3. *Cerebrospinal cases*, including transient or permanent paralyses, such as hemiplegia, paraplegia, loss of bladder and rectal control, represented 2.16 per cent.

4. *Dyspnea*, called “chokes,” of a type resembling an asthmatic attack, occurred in over 1.5 per cent., and may well be due to multiple small gas emboli in the pulmonary vessels; for were it of central nervous origin it would naturally be accompanied by other serious nerve disturbances, which is not the case.

5. *Prostration* of moderate degree associated with pains in some some part of the body made up 1.25 per cent.

6. *Collapse*, with partial or complete unconsciousness happened in about 0.46 per cent.

7. *Fatal cases* were 20 in number, or 0.54 per cent., and occurred either with rapid onset of unconsciousness and collapse; or with pains and prostration, accompanied by nausea and vomiting; or with paralyses; or from later complications of persistent paraplegia.

CLASSIFICATION OF SYMPTOMS (Acute). The symptoms of aeropathy will vary with the anatomic part affected, with the amount of gas set free, and the consequent degree of disturbance of function.

Connective tissue, especially fat, with its peculiar ability of absorbing four times more nitrogen than other tissues, and its

poor blood supply, becomes desaturated more slowly than other body tissues; and it is found in practice that fat men are ill adapted to work in compressed air.

Proceeding therefore to tabulate symptoms with reference to the structures affected, we find symptoms referable to the following:

1. NERVOUS SYSTEM. (a) *Peripheral Nerves*. Pain occurring in the extremities or abdomen in over 88 per cent. of all cases, without other evidence of spinal-cord irritation, except in a little over 2 per cent., must admittedly be due to peripheral irritation of nerves and nerve terminals by bubbles of gas in the nerve sheath, in fascial tissues, beneath the periosteum or in bone-marrow, etc.

Numbness, anesthesia, and paresthesia are doubtless capable of the same explanation.

One form of paresthesia, called by the workmen "itch," is quite common, is distressing while it lasts, but is never of serious import. This may be explained, as Hill does, as due to bubbles in the subcutaneous areolar tissue; but in my experience it is no more common in fat men than in thin men; it occurs especially when sweating has been less free, and it is usually at once relieved by a hot bath or sweating, all of which make it more probable that it is caused by expanding bubbles in the sweat glands.

(b) *Central Nervous System*. Brain: Unconsciousness, stupor, and collapse may be due to cerebral gas-embolism or the resulting edema, or are secondary to circulatory failure due to coronary or pulmonary embolism.

Cerebral gas-embolism may also cause temporary aphasia, incoherence of speech, ataxia, vomiting, vertigo, headache; or such signs as hemiplegia, monoplegia, convulsions, nystagmus, and tongue deviations, depending upon what area is affected.

Actual tearing of nerve tissue and hemorrhage may arise from the expansion of bubbles of gas, resulting in organic lesions.

Spinal Cord: Affections of the spinal cord include paraplegia, monoplegia, loss of bladder and rectal control, partial paralyses, spasticity, exaggerated, diminished, or absent reflexes; anesthesia, anesthesia dolorosa, etc.; and with hemorrhage into the cord the symptoms may become permanent and a true myelitis may develop.

Frequently, however, there is only a temporary weakness and numbness of the legs, with or without retention of urine.

2. SPECIAL SENSES (a) *Eye*. Transient blindness, diplopia, and nystagmus may occur.

(b) *Ear*. Perforation of the drum membrane may occur, but only during compression, hence it is not properly a symptom of aeropathy. Deafness and vertigo may follow the formation of bubbles in the labyrinth or hemorrhage in the same situation.

3. VASCULAR SYSTEM. Gas emboli in the veins of the systemic and portal system, in the right heart, in the pulmonary and coronary vessels, have been found so regularly in animal experimen-

tation and at autopsies upon fatal cases among men (provided the autopsy be performed within twenty hours after death from an acute attack) that this fact forms the whole basis of our understanding of the etiology of this disease. The bluish "mottling" of the skin, seen over the chest and abdomen in some of the more severe cases, is caused by embolism of the superficial veins, with consequent stasis.

Lymphatic obstruction by gas embolism is doubtless the explanation of the several instances of localized edema of a small area of an extremity.

4. **RESPIRATORY SYSTEM.** The symptom called "chokes" has been described above. In certain fatal cases there has been found edema of the lungs, also interstitial emphysema of the parenchyma.

5. **GASTRO-INTESTINAL SYMPTOMS,** further than the epigastric pains and the nausea and vomiting above mentioned, are not encountered.

6. **INTERNAL ORGANS,** such as the liver, spleen, kidneys, do not give any acute signs, although at autopsy they may be found affected.

7. **THE SEXUAL APPARATUS** is only affected as a result of spinal-cord injury, which may give rise to priapism, etc.

8. **THE BONES, JOINTS, AND PERIOSTEUM.** In one case necrosis of the femur resulted apparently from thrombosis of the medullary artery. The deep-seated pains so frequently referred to the long bones of the extremities and to the joints may be due either to collections of expanding bubbles under the fascial planes or under the periosteum; or, as Hill suggests, in the yellow marrow, which structure is rich in fat and deficient in circulation.

9. **THE SKIN AND SUBCUTANEOUS TISSUES.** The symptoms of "itch" and the "mottling" of the skin have been described above. Subcutaneous emphysema, without trauma, is met with in a few cases during life, and frequently in autopsies, especially along the course of the large veins of the extremities. Its presence as an accompaniment of contusions and punctured wounds I have several times demonstrated, and it is doubtless due to the setting free of gas from the extravasated blood; for it is hardly likely that such an amount of compressed air could enter through the puncture.

10. **LOCALIZED COLLECTIONS OF GAS,** aside from the small emboli scattered through the body, include the large collections found in the right side of the heart at autopsy (case cited below). At one autopsy which I witnessed there was a collection of about 5 c.c. of gas beneath the mucosa of the jejunum. In two other cases I succeeded in aspirating about 1 c.c. of gas from beneath the periosteum of the tibia; its presence was evidenced by a soft cushion-like swelling in this area.

11. **MISCELLANY.** In general wounds bleed as freely and heal as readily in the compressed air as in the normal atmosphere.

Infections of the middle ear and of the sinuses which communicate with the nose are favored by the efforts of men to force open the Eustachian tubes during compression, which factor also accounts for most of the infrequent cases of epistaxis in caisson work.

In the use of the diving helmet, however, bursting of the air tube may cause epistaxis, ecchymoses, ruptured eardrums, etc., by the cupping effect of sudden removal of pressure from the upper part of the body.

Cystitis, pyelonephritis, myelitis, and meningitis may occur as sequels of cord injury, but are not properly among the acute effects.

CONCLUSION. In a paper so limited little more than an outline of the acute effects of aeropathy is possible. In conclusion therefore I would report what is I believe the first analysis ever made of the gases found in the right heart of a man who died from the effects of this disease.

November 19, 1907, with the assistance of Dr. J. E. McWhorter, we collected 3.1 c.c. of gas by aspiration from the right heart at the autopsy, fourteen hours post mortem, of a man who died in one hour after a seventeen minute decompression, following eight hours' exposure to +30 pounds pressure. Upon analysis this gas yielded nitrogen 80 per cent., CO₂ 20 per cent., which percentages are in accord with analyses made in animal experiments by various writers on this subject.

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THE LATE MANIFESTATIONS OF COMPRESSED-AIR DISEASE.¹

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In this paper attention is called to the ailments met in compressed-air workers years after the exposure and acute manifesta-

¹ This work was partly conducted under a grant from the Otho S. A. Sprague Memorial Institute. Read before the XVth International Congress of Hygiene and Demography in Washington, September 24, 1912.

tions. The material is practically the same as that which formed the basis of the article on compressed-air disease in the "Report of the Commission on Occupational Diseases of Illinois" (published in Chicago, 1911). An abstract of this report, read before the Chicago Neurological Society,² is as follows:

"Some of the men examined had had their acute attacks many years ago; others during the present year. Of the 161 men, 87 had various affections of the ears, causing permanent impairment of hearing in 65 cases; 141 gave a history of "bends," that is, severe muscular and articular pains; 34 had paralysis, most generally transient and affecting the legs, although 3 men have permanent partial paralysis of one arm and 3 of both legs; 11 present more or less chronic joint pain and stiffness. One of these men who developed an affection of the hip immediately after working his second shift in compressed air twelve years ago has been an invalid ever since, and presents the typical x-ray picture of arthritis deformans. He had been in perfect health before these two exposures to compressed air. One man with signs of caisson myelitis had a spontaneous fracture of the patella eleven years after the acute attack which had consisted of numbness in both lower extremities, followed by pain; 12 men now present signs of some degree of permanent cord disease; 13 were delirious or unconscious during the acute attack; 33 complained of vertigo as a prominent symptom; 6 of vomiting during the acute stage; 11 of incontinence or retention of urine; 5 had numbness without paralysis; 6 had "blind staggers," that is, labyrinthine vertigo, with nystagmus; 2 had "chokes." Several men gave a history of large swellings of the soft part of the chest wall or in the vicinity of joints. Bassoe had not seen them at this stage, but agrees with Heller, Mager, and Schrötter that the swellings are due to vasomotor disturbances of central origin, not to local liberation of gas (*tumeurs gazeuses*), as has been claimed by French writers. He considers the nitrogen-bubble theory of Paul Bert fully proved by both the observations on human beings and the abundant experimental work recorded in the literature. The cases treated by immediate "recompression" had fared much better than those not so treated."

Early in 1912 a number of these men were subjected to renewed and more thorough examination. They naturally group themselves in three classes, which will be taken up separately and illustrated by case records:

I. Cases in which spinal cord symptoms predominate: "caisson myelitis."

II. Cases of permanent joint affections, with the clinical and x-ray picture of arthritis deformans.

III. Cases of permanent ear affections.

² Jour. Nerv. and Ment. Dis., June, 1911.

Naturally some men present symptoms belonging in two or all three of these classes, but, as a rule, one set of symptoms predominates.

CLASS I. CASES OF "CAISSON MYELITIS."

Group A. *Cases with signs of trophic osteo-arthropathies dependent on the cord lesions.*

CASE I (Illinois report, Case 23).—Attack of "bends," with numbness of legs and stiffness of knees, in 1898; spontaneous fracture of patella in 1909; porosis and atrophy of fragments; fracture of external tuberosity of humerus in 1911. Signs of cord disease.

Male, aged forty years. Fourteen years ago he worked on Oak Street Water Tunnel, in eight-hour shifts. Pressure, twenty-eight to thirty-two pounds. After working for a week he had the first attack of "bends." Decompression three and a half to five minutes. Five and a half hours later was taken with numbness and cold feeling in both lower extremities from the hips down, followed by severe pain for six or eight hours and stiffness in the right knee. He returned to work in two days and then the knee felt better, but it has never been well since. In January, 1909, on getting up from a chair, the right patella was fractured and an abscess formed. He was laid up for five months. In August, 1909, he fell four feet and cut the skin over the right knee. On another occasion, on coming out from the lock, he had bleeding from the nose and ears. He returned to the lock and the trouble stopped. He has also worked on the Illinois Tunnel and the Four Mile Water Tunnel without trouble. He denies syphilis, but admits gonorrhea. He states that from the time of the acute attack of "bends" until the patella was fractured he had only slight pain.

Examination in October, 1910: Pupils normal. The right knee is stiff; there is a scar across it and there is palpable evidence of an old fracture of the patella. Ankle jerks absent; left knee jerk absent; right knee jerk cannot be tested on account of limitation of motion. On stroking the sole of the foot extensor response of the right big toe is obtained, and flexor response on the left side. Sensation normal. No sphincter disturbance.

Dr. Hollis E. Potter took an x-ray picture of the right knee and reports the following findings: "Fracture of the right patella at a point just below the middle of the bone. Diastasis of fragments of two inches. A third and smaller fragment lies between the two main portions. The lower fragment is elongated at the point of rupture. All surfaces of the fragments as now seen are rounded off, leaving no angles or corners. All fragments show porosis and bone atrophy."

In the spring of 1911 he fell on the floor on his left hand and sustained a fracture of the greater tuberosity of the humerus.

He admits rather heavy drinking, which probably accounts for an enlargement of the liver, which was quite marked when he was reexamined in April, 1912. Then the right knee was found to be more freely movable, while there was slight limitation of motion at the right ankle. The knee and ankle jerks were now obtained on both sides, the former even exaggerated. The right knee jerk was stronger than the left, and the right-sided Babinski sign persisted. No ataxia. Sensation normal. Blood pressure equals 150 mm. of mercury. Urine normal.

CASE II (Illinois report, Case 59).—"Bends" in right knee in 1890; lame ever since; looseness of patella, with atrophy of bone; disturbances of reflexes and sensation.

(Cousin of Case I.) Male, aged forty-five years. Twenty years ago he worked on the Four Mile Tunnel at a pressure up to twenty-five pounds. He had several light attacks of "bends," and then, after he had been in the tunnel at a pressure of twenty-five pounds for about twenty-five minutes, he was taken with nosebleed, and five minutes later with bleeding from the left ear. He went out through the lock in one or two minutes, and on coming out bled from both ears. While still in the lock he had severe pain in the left temple and the left side of the forehead. After coming out the pain was less severe, but he was dizzy. Twenty-four hours later he was taken with severe pain in the right knee, which lasted for seven months. He was in the Cook County Hospital and two other hospitals on account of the pain, which later particularly involved the left knee and left arm. Twenty-seven months after the onset he went to work as an elevator man in the Cook County Hospital. He did this work for three months and gradually improved. Three years ago he tried to work in compressed air at Gary, Indiana. The pressure was seventeen pounds, and he only worked one shift, as he developed a peculiar sensation in the left arm.

He still limps, dragging the right leg. In the spring of every year he has more pain, and he then often has noticed that the right patella appears to be very loose. The left arm is numb in the region of the elbow. He has had no sphincter disturbance. He works most of the time, but can only do lighter work.

The watch-tick is heard at two inches in the left ear and at four inches in the right ear. Wrist jerks are absent, the elbow jerks diminished; abdominal reflex not obtained. The right cremasteric reflex is stronger than the left; the knee jerks are increased; the plantar reflexes are normal. The right ankle jerk is diminished; the left not obtainable. Tactile and pain sense are moderately diminished in both legs, especially on the outer surfaces. The right lower extremity is two inches shorter than the left, and the circumference of the right thigh is two inches less than that of the left, while the circumference of the right calf is only one-half inch

less than that on the left side. The right patella is slightly more movable than the left.

On account of the looseness of the right patella the patient was referred to Dr. Hollis E. Potter for x-ray examination of the right knee. Dr. Potter's report is as follows: "The noticeable feature is a lateral widening of the upper face of the tibia, allowing a projection of one-half inch of this bone beyond the articular surface of the femur. It is difficult to account for this, since all profiles of both bones are smooth and regular, excepting a slight roughening of the inner condyle of the femur on its articular surface, suggesting cartilaginous loss. Slight atrophy of patellar borders."

Many years ago he injured the right eye in a dynamite blast, and the right pupil has been dilated ever since. Formerly the pupils were equal and the eyes normal in every way, according to the patient's statement.

CASE III (Illinois report, Case 37).—Repeated attacks of "bends" for twenty-seven years; paralysis and incontinence in 1910; signs of cord disease; islands of atrophy and of sclerosis in tibia.

Male, aged forty-six years. He has worked in compressed air in various places since seventeen years of age. Had "bends" lightly in New York and New Jersey, worse in Cleveland, where the pressure was forty-eight pounds, and where he worked in two-hour shifts, at intervals of four hours. After exit in four minutes he was taken with severe pain in the legs and arms and was in a hospital for four weeks. He could not stand high pressure well afterward; developed the "bends" again, and left Cleveland. When working on the Four Mile Tunnel in Chicago, at a pressure of twenty-seven to thirty pounds, he had slight "bends" after coming out through the lock in about three minutes, and he had to abstain from working for three days on account of the pain. In 1910 he worked at Hibbing, Minnesota, where an ore shaft was sunk. Pressure, thirty-eight to forty pounds. After his first shift of two hours on January 20, he came out through the lock in about one and a half minutes, although the posted order of the company was that the time should not be less than fifteen minutes. But there was a "green" lock-tender. Immediately after exit he had severe pain in the abdomen and extremities, could not walk, and at the same time the left ear-drum was ruptured, with bleeding from the ears. He was placed in the hospital lock, without relief; then he had a hot bath, and was placed in the hospital lock a second time. He was in the hospital for three weeks, and then stayed five weeks at the hotel, unable to work. He could not walk for seven weeks after the onset, and had incontinence of urine and feces until a few months before being seen in October, 1910. At that time urination and defecation were still precipitate, and he still had some weakness and pain in the legs. He could not hear watch-tick when the watch was in contact with the left ear; barely heard it in the right ear.

Knee jerks were normal or slightly exaggerated. Right ankle jerk was absent (left not tested). He did not feel pinpricks in the legs and hands. He said that when examined at the hospital at Hibbing he could not feel pinpricks.

When seen again, in April, 1912, he had not been in compressed air since the previous examination. He had worked some, but was troubled with pain in the right leg and occasional incontinence of urine and feces; of the former, especially after drinking beer. The right leg sometimes "gave way" when he walked, but recovered after a brief rest. The right ankle was considerably stiffened, while there was normal range of motion in the other joints. There is now distinct analgesia only of the outer part of the left foot, and the outer aspect of the lower third of the left leg. No Romberg sign. Blood pressure equals 100 mm. of mercury.

X-ray examination by Dr. Hollis E. Potter fails to show any bony change to account for the stiffness of the right ankle. There is no change in the tibia within an inch of the ankle-joint, but from this level and extending upward there are irregularly shaped islands of atrophy and of sclerosis in the interior of the bone. There is also mushrooming of the anterior portion of the astragalus into the scaphoid, resulting in flat-foot.

Group B. *Very Limited Persistent Cord Lesions.*

CASE IV (Illinois report, Case 110).—Two attacks in 1896; permanent sensory loss in left ring and little fingers.

Male, aged fifty-two years. About 1896 he worked for six months in compressed air at the Sixty-eighth Street Tunnel in Chicago. He had two attacks. The first one occurred after coming out from a pressure of twenty pounds. He had severe bursting sensation in the head, nosebleed, ringing in the ears, and dizziness. On returning to compressed air he was considerably relieved, but on coming out the second time the ring and little fingers of the left hand became numb. He could move them, but they were evidently analgesic, as four months later a piece of flesh was accidentally torn out of the little finger without causing him any pain. The right heel also became numb in this attack, and remained so for about six months. He stayed away from work one week. The second attack occurred a month later, and consisted of similar sensations in the head. He again improved on returning to compressed air. The condition of the affected fingers and heel was not changed by this attack. He lost two shifts. A few years later he worked on the Oak Street Tunnel, and had no trouble except that he was "blocked" a few times. He quit compressed-air work and now works at a pumping station.

Examination in 1910 revealed diminished tactile, pain, and temperature sense of the left ring and little fingers, and of the ulnar side of the hand and forearm, more so on the extensor surface. The wrist, elbow, knee, and ankle jerks were normal. The watch-

tick was heard at eight inches on the left side, twelve inches on the right side, and he is now in good health.

When reëxamined in June, 1912, he still complained of "sleepy feeling" in the same fingers and in the ulnar portion of the hand. The anesthesia remained, and there was also loss of the sense of passive motion in the affected fingers.

CASE V (Illinois report, Case 107).—Attack of pain in right hand and forearm in 1898; persistent analgesic area on forearm.

Male, aged thirty-nine years. In 1898 he worked on the Sixty-eighth Street Tunnel, Chicago, and after working three months he had an attack while at work, at a pressure of eighteen to twenty-four pounds. He was taken with pain in the fingers of the right hand, which ascended to the elbow, and was very severe. He went out through the lock in three or four minutes, which was unusually slow, and then became dizzy and had ringing in the ears. The pain remained about the same and lasted for five weeks. He went to work after ten weeks, but not in compressed air until working on the Thirty-ninth Street Tunnel about three years later. The pressure here generally was twelve pounds, and he had no trouble.

The right arm has been a little weak ever since the attack, and occasionally there is a "stitching" pain in it after a hard day's work. On examination the arm reflexes and tactile sensation in the arm are normal, but there is an analgesic area in the inner half of the upper third of the anterior surface of the right forearm. Knee and ankle jerks increased without clonus. Watch-tick heard at four inches in the left ear, ten inches in the right ear.

When seen again in March, 1912, he said he had been forced to give up his work as a bricklayer's tender because heavy lifting would cause pain and subsequent "falling asleep" of the right arm from the elbow down.

Three other cases of this kind will be placed in Class III on account of the more important joint lesion (Cases XII, XIII, XV).

Group C. *Cases of Ordinary More or Less Extensive "Caisson Myelitis."*

CASE VI (Illinois report, Case 8).—Onset in 1890; persistent pain in the legs and precipitate micturition; changes in the reflexes.

Male, aged fifty-four years. First seen in July, 1910. He worked under compressed air on the Four Mile Tunnel, Chicago, from 1890 to 1893, and had charge of the bricklaying. He had the "bends" three times. The first time after an eight-hour shift he came out from a pressure of twenty-two pounds in two or three minutes, although he had been advised by the engineer in charge to spend ten minutes; but this precaution was seldom taken. In half an hour he was taken with severe pain in the knees, shoulders, and wrists, became dizzy, fell down in the street, and was picked up by a policeman, who thought he was drunk, until informed to the

contrary by other workmen. He returned to work the next day. The second attack was similar, starting with pain in the knees, then he was dizzy and slightly dazed. He returned to work the next day. The third attack came on one-half hour after less than five minutes' decompression after an eight-hour shift in pressure of thirty-three to thirty-five pounds. He was attacked with dizziness and pain in the knees. Was taken home, stayed in bed for about thirty-six hours, was not clear mentally, sat up in bed, and "mumbled." He returned to work in a week, but the legs were weak and aching and the back was painful on stooping. There was no sphincter disturbance at first, but in a few weeks he developed precipitate urination, which grew worse and became permanent. He had to give up work, and was a patient in the Cook County Hospital from February to May, 1895. His case then seemed to have attracted considerable attention. He has never recovered, has suffered much pain, and walks very poorly. Has not been able to work at his trade since then, and has been idle most of the time; but at the time of examination had an easy position as night watchman. He was in perfect health before working in compressed air, but has been a heavy drinker. On examination there is found opacity of the left cornea. The right pupil reacts to light. Hearing in the right ear is defective, the watch-tick only being heard on contact. In the left ear it is heard at three inches. He cannot get the right heel down to the floor except when the left heel is raised. The left knee jerk is considerably exaggerated, but the right is about normal. Both ankle jerks are diminished, the left more so. Arm reflexes normal. Sensation normal. He died suddenly in 1911.

CASE VII (Illinois report, Case 155).—Four attacks of "bends," one associated with transient paralysis of both legs and retention of urine. Increased reflexes and sensory disturbance.

Male, aged twenty-four years, was seen in November, 1910, at St. Louis, where he was working in caissons for the new bridge. He had worked in compressed air since 1903. The first attack was in 1907, and came on after working at a pressure of twenty-two pounds. The decompression lasted seven minutes, and ten minutes later he was taken with severe pain in the left knee. He was well in two days and had the second attack six months later, after coming out from a pressure of twenty-eight pounds in ten minutes. He had pain across the abdomen, and "knots" formed in the abdominal muscles. Both legs were paralyzed for two hours and he had to be catheterized for two weeks. For the next six months there was some dribbling of urine, and since that time the legs "fall asleep" easily. He returned to work in a month and worked two three-hour shifts at a pressure of thirty pounds in one day. After coming out from the second half in ten or twelve minutes he was immediately taken with pain in the abdomen.

He took a bath and was then suddenly attacked with extreme dizziness, tinnitus, and nausea. He could not see plainly; everything seemed to whirl around. He did not vomit until a physician gave him medicine, which he thinks was an emetic. He was in the hospital for ten days; could walk after four days, but some dizziness remained for two months. Tinnitus and complete deafness were present the first three days, and hearing has never been normal since. Then he had a couple of attacks of "bends" while working on two bridges in Arkansas. The first one was slight and affected the hips; the second one was rather severe, affected the left arm, and he did not fully recover for a week. Since February, 1910, he worked on the bridge at St. Louis, and in April, while working two daily two-hour shifts at a pressure of forty pounds, he had an attack. Decompression lasted fifteen minutes, following which he was taken with pain in the left hip, which lasted all night, and finally, was relieved in the hospital lock, but he had to go in and out four times. Aside from these definite attacks he has frequently had some burning in the skin of the abdomen and of the left arm after coming out. This has occurred as a regular thing when the pressure was high. He has also frequently been dizzy for about ten minutes after coming out.

Watch-tick heard in right ear at three feet; in the left ear not heard on contact, but C-2 tuning-fork is heard. Both knee and ankle jerks are exaggerated, and there is reduced pain sensation in the left leg.

In this connection the following case is of interest as showing how repeated attacks with severe acute symptoms may fail to produce any permanent disease:

CASE VIII (Illinois report, Case 147).

Male, aged thirty-six years; foreman. Seen at St. Louis in November, 1910, where the following record was made: Has worked in compressed air for ten years, much of the time as foreman or superintendent; has made his own rules, and has stayed much longer in and come out more quickly from the compressed air than the ordinary laborers are permitted to do.

The first attack occurred at Canadian, Texas, in 1905. He stayed in a caisson, which had sunk, for one and a half hours at a pressure of fifty-three pounds, and came out in about five minutes. Then stood out in the cold air for a while, and after fifteen minutes suddenly became paralyzed from the waist down. He had no pain, could not move the legs for eight days, had to be catheterized for ten days, and required enemas to move the bowels. He then improved rapidly, but had severe pain in the knees and ankles for four days after recovering from the paralysis. He had full control of the bladder after the retention ceased, but there was burning on micturition for some time. The catheter had not been boiled, and had been passed by a "sand-hog." The next attack

occurred in Arkansas one year ago, after he had spent twelve consecutive hours in a pressure of forty pounds. He came out as rapidly as the valve would permit, and had severe pain in the right shoulder for two days. He had no trouble when working on the Traction Bridge at St. Louis, but has had two attacks while working on the new bridge since last February. The first one occurred on the Illinois side last September. He spent seven hours at a pressure of fifty-one and one-half pounds, and came out in three and one-half minutes, while the time prescribed for the men was thirty-five to forty minutes. Five hours later, when in bed, he was taken with slight pain in the knees, and one hour afterward became paralyzed from the waist down. He was placed in the hospital lock forty-five minutes after the onset of paralysis, and movement returned in thirty-five minutes. He stayed in the hospital lock for about eighteen hours, and then was well and returned to work. The second attack also occurred on the Illinois side, on October 25. He stayed in a pressure of forty-five pounds for several hours, came out in three to five minutes, and half an hour later was taken with pain in the right shoulder. He used hot applications without any benefit, and two hours later he went to the hospital lock, where he remained for seventeen hours, during which he had no relief at all, and after coming out he was worse than before. The arm is still weak and hurts a little. There was no swelling. Reflexes and sensation in both arms normal. Knee jerks brisk.

CLASS II. CASES OF PERMANENT JOINT DISEASE OF THE TYPE OF ARTHRITIS DEFORMANS.

In the course of this investigation several cases were observed in which chronic arthritis of one or more joints had developed as a sequel of "bends" in the vicinity of the joints affected. The histories are so explicit on the point of the origin of the joint trouble in attacks of articular pain immediately following exposure to compressed air that it seems an etiological relationship must exist. In some of the cases (XII, XIII, XV) acute cord symptoms as well as persistent ones were present, so as to make it possible that we are dealing with the osteoarthropathies previously considered, while in others it seems simpler and more reasonable to assume that the joint changes are the result of trauma to the articular structures by the local liberation of air—a well-recognized and common phenomenon.

CASE IX (Illinois report, Case 47).—Typical arthritis deformans of right hip; onset in 1899 after working only two shifts.

Male, aged sixty-nine years; carpenter. Twenty years ago he worked on the Four Mile Tunnel in Chicago without trouble. Eleven years ago he did some carpenter work in the Oak Street Tunnel and worked two eight-hour shifts under a pressure of about thirty pounds, from which he came out rapidly. On the way home

from the last one he was taken with pains in the legs, which became extremely severe and lasted all night. He says that he was blue all over the body and the physician could not feel his pulse. The blueness disappeared after rubbing the skin. He went to work in four days, but the legs were weak, especially the right one. He has walked lame ever since on account of pain, which is chiefly felt in the right groin, and especially comes on when he starts walking. A year after the onset he saw the late Dr. Christian Fenger, who put on an extension apparatus for ten weeks. Then he felt worse and had to use crutches for a year. He has not worked since this time. He never had any rheumatism, and was in good health before this occurrence. The knee jerks are brisk and the ankle jerks normal. Sensation and plantar reflex in the right leg normal. He had no sphincter disturbance, but now has to get up at night to urinate. There is an apparent lengthening of the right leg, which he says has been present ever since the extension apparatus was used.

Dr. Hollis E. Potter took an x-ray picture of the right hip and reports the findings as follows: "All changes are compatible with an arthritis deformans of the hip-joint, namely: The head of the femur is flattened and mushroomed; the neck of the femur appears shorter and wider; cartilaginous space decreased; osteophytes laid down at edges of cartilage, acetabulum, and head of femur."

The above notes were made in October, 1910. When last seen in May, 1912, the condition of the hip remained the same. The distance from the anterior superior spine to the inner malleolus was the same on both sides, but that from the umbilicus to the inner malleolus was 1.5 cm. greater on the right side. There was limitation of motion in the right hip in all directions.

CASE X (Illinois report, Case 115).—Attack of "bends" in 1901, at once followed by pain in the right knee and a couple of years later by pain and stiffness of the right hip. Typical advanced arthritis deformans of the latter.

Male, aged forty-eight years. In 1901 he worked on the Thirty-ninth Street Tunnel without trouble. Then in Cincinnati for three months in 1902. His first shift was six hours at a pressure of fifty pounds. He came out through two locks, spending five minutes altogether. One and a half hours later he was taken with severe pain in the right knee, chiefly located at the inside of the patella. It was severe for three days. Neither hospital lock nor a bathtub was available. He has had more or less pain in the right knee ever since. He became unable to bend the knee fully, and could only walk a few blocks. He worked as a bricklayer until 1905, and since then has been a masonry inspector for the city. He has been in compressed air occasionally, but has had no further attack. Two or three years after the acute attack he also developed pain

in the right hip, and this joint gradually became stiff. He has been considerably better during the last one and a half years, and ascribed the improvement to massage. Examination revealed marked limitation of motion in the right hip. The knee and ankle jerks are exaggerated, slightly more so on the right side. Sensation in the lower extremity is 'normal, but he complains of occasional sensation of pins and needles in the soles of the feet, and sometimes the fingers become white and feel a little numb. When standing long the pain in the hip and knee gets worse, and the thigh feels numb. X-ray picture of the hip taken by Dr. Max Reichmann in 1912 shows the joint partly obliterated by bony hypertrophy along the acetabular margin and at the base of the head of the femur. There is plastic overgrowth of bone at the upper margin of the neck. There is slight upward wandering of the acetabulum compatible with shortening of one-half inch. The condition is typical of advanced arthritis deformans of the hypertrophic type secondary to an atrophic state.

CASE XI (Illinois report, Case 72).—Attacks of bends and vertigo in 1905; since then repeated joint swellings; x-ray findings typical of arthritis deformans in knees and ankles; areas of atrophy and sclerosis of bone in right fibula.

Malc, aged forty-one years. In 1905 he worked for nearly a year as timekeeper at the East Boston Tunnel. Pressure variable; maximum, twenty-six pounds. After working ten weeks he had his first attack after coming out from a four-hour shift at a pressure of twenty-six pounds in eight or ten minutes. Immediately after exit he was taken with dizziness, bleeding from nose, ears, and eyes, pain in the knees and ankles, and across the small of the back. He was taken home in a carriage and stayed in bed for four weeks, during which the pain was continuous and severe, especially in the back. He could move the legs, but could not get up on account of the pain. Urination was slow, followed by dribbling, and has remained so. Sexual power not affected. Some dizziness and tinnitus, especially on right side, have persisted. He returned to work in six weeks, but could do very little. Two weeks later, after coming out in ten or twelve minutes from a pressure of twenty-four pounds, he was again taken with dizziness, nosebleed, and pain in the knees and back. Stayed in bed three weeks. After another week he went to work, but never returned to compressed air, and has worked as a salesman and insurance agent. He has become generally nervous, suffers considerably from pain in the back and knees, headache, and tinnitus, the latter particularly during colds. Occasionally there is swelling of the knees and ankles, all of which joints became swollen within a few hours after exit from the lock at the time of the attack. These joints now become swollen about once a month, usually all four at a time, and the swelling lasts from a few days to two weeks.

The watch-tick is heard in the right ear at six inches, left ear at twelve inches. Knee and ankle jerks normal. There is much tenderness about the knees and a grating is felt when the patellæ are moved.

When last seen, June, 1912, he stated that he had been in bed for a month during the winter on account of pain and swelling of the knees, ankles, and hands. Grating in the knees, especially the right one, was still present.

X-ray pictures of the right knee, as interpreted by Dr. Hollis E. Potter, show deposition of bone at the upper anterior surface of the patella, "lipping" of the tibia anteriorly, and external displacement of the tibia on the femur, the joint surfaces not being in perfect apposition. The right ankle shows fragments of bone at the extreme lower end of the fibula, but it is not clear whether they are derived from the fibula, astragalus, or ossified ligaments. The lower half inch of the fibula shows irregular areas of atrophy and sclerosis. The left ankle shows little change, merely slight atrophy of the extreme tip and inner surface of the fibula adjacent to the astragalus. The hands show no changes.

CASE XII (Illinois report, Case 111).—Attack of "bends" in 1896, both shoulders affected; now pain and stiffness of left shoulder; anesthesia over left scapula; x-rays show arthritis deformans of left shoulder.

Male, aged forty-three years. First seen in October, 1910. About twenty years ago worked as a bricklayer on the Four Mile Tunnel, Chicago. Pressure eighteen to twenty-one pounds. He worked seven and a half hours a day at one stretch. One attack occurred after coming out in three to three and a half minutes. He first had twitching in the muscles of both arms, and half an hour later severe pain in the same locality, which lasted for about eight hours. The next attack occurred in 1896, after he had been working for two weeks on the Cleveland Tunnel. He came out in about two and a half minutes from a pressure of thirty-four pounds, in which he had worked continuously for nine hours. At once he was taken with severe pain in the chest and both shoulders. He went back in the lock for two hours, during which he was relieved, but after coming out the second time in four or five minutes the pain returned. Then he was again relieved by staying in a warm bath for six hours, but the pain returned and lasted about four days. He then returned to work and had no pain while in compressed air, but ever since this attack he has frequently had twitchings and pain about both shoulders and across the chest, when not in compressed air. The trouble is now diminishing, and he only has it occasionally, when resting after a hard day's work. It is now only felt in the left shoulder. He is now a sewer inspector. He had no rheumatism of any kind before this attack. He denies syphilis, but admits gonorrhea. Examination revealed consider-

able limitation of movement in the left shoulder. He cannot raise the arm fully to the vertical position. The arm reflexes are normal. There is a triangular area of tactile anesthesia above the spine of the left scapula. The temperature sense is also diminished in this area and downward to the level of the angle of the scapula. Pain sense is lost in the triangular area, but is not affected as far downward as is the temperature sense. Sensation on the arm and chest normal.

When reëxamined in 1912 the findings were practically the same, the anesthetic area extending from the edge of the trapezius nearly to the angle of the scapula.

X-ray examination of the shoulder by Dr. Max Reichmann shows the head of the humerus to be enlarged and porotic. There is great irregularity in the joint surfaces, and the rim of the glenoid cavity is greatly overgrown with bone.

CASE XIII (Illinois report, Case 5).—Pain in legs and paralysis in 1897. Limitation of motion in hips. Articular pains since onset. Altered reflexes.

Male, aged forty-eight years; bricklayer. In 1897 he worked in compressed air during the construction of a water tunnel at Rockford, Illinois. The pressure was thirty-nine pounds, and he worked in two long periods. He thinks decompression lasted about five minutes, as only a one and one-half inch valve was used. After coming out from his third shift he was immediately taken with pain in the legs, walked to his boarding house, became paralyzed in the legs, and was taken to a hospital in Rockford, where he remained for three days, during which there was much pain. He was then taken back to Chicago, but could not walk at all for six months. During this time he could move the legs a little, but every movement caused pain and the muscles often felt "as if tied in a knot." There was no sphincter disturbance at first, but about a year and a half later micturition was slow and rather painful for a time. He has never been entirely free from pain since the acute attack, and had to give up bricklaying altogether. The pain affects the knees, thighs, and hips, and is generally worse in the autumn of every year. He has done a little work as inspector for the city and some light work in tunnels, but recently he has been quite lame and unable to do any work. Of late he has had considerable edema of the legs.

The pupils are equal and react normally. The knee jerks are slightly increased. The ankle jerks cannot be obtained, while the wrist and elbow jerks are increased. Abdominal and cremaster reflexes normal. Sensation normal. Considerable stiffness, pain, and limitation of movement in both hips. The strength in the muscles of the legs is fair. Heart normal. The urine contains considerable albumin.

CASE XIV (Illinois report, Case 58).—In 1899 attack of pain in legs, vertigo; rupture of ear drum and persistent deafness; left knee still painful.

Male, aged forty-three years. Seen in October, 1910. He first worked under a pressure of nine to fifteen pounds on the Illinois Tunnel in 1899. On one occasion, when the pressure was nineteen pounds, he had a bursting sensation in the ears while in the lock, and had bleeding from both ears, nose, mouth, and eyes. He became extremely dizzy and partly unconscious; was carried out and taken to the Polyclinic Hospital, where he stayed for three days, during which time he was very dizzy. The left drum was found to be ruptured; the bleeding lasted for about an hour and a half, when there was purulent discharge from the left ear for six or seven months. He also had pain in the limbs and back, and had to be helped to raise himself in bed. He had much backache for four months, and there was left tinnitus, like the ringing of bells, for two years. Hearing in the left ear has been lost ever since. Three years ago he worked in compressed air at Clinton, Iowa, but he had to give it up on account of dizziness and queer feeling in the head. Both knees, especially the left, have been quite stiff ever since his first attack. He had then returned to work in six months, shoveling earth, but had to quit in less than a week on account of pain in the knees, arms, and back. The left knee now is painful on passive movement and on tapping the patella. The knee jerks are normal. The left ear is totally deaf, not even a C-2 tuning-fork is heard. Watch-tick heard in right ear at one foot.

CASE XV (Illinois report, Case 160).—Ear trouble since "blocked" in 1898; three attacks of "bends" in 1901; still often pain in knees and ankles; x-ray of left knee shows islands of sclerosis in tibia and thickening of surface of tibia; diminished sensation and decreased reflexes in legs.

Male, aged thirty-five years. First seen in October, 1910. In 1898 he worked on Illinois Tunnel, under a pressure of eighteen pounds. Bled from right ear when going through lock the first time. He returned to work the next day, but had tinnitus for a week, and the right ear has been slightly deaf ever since. Whenever he had a cold this ear would trouble him when he went into compressed air. In 1901 he worked for one year in Cleveland, Ohio, Water Tunnel, where he had three attacks. The first one occurred after he had been working for three weeks. One hour after very rapid decompression following an eight-hour shift at thirty-seven pounds he was taken with pain in both legs, "like a sword tearing up and down the flesh," which lasted eighteen hours. He was out of his head on account of the pain—"would have killed himself if he had the chance." He was given plenty of hot whisky, and returned to work in five days. Two other men were affected at the same time. The second attack occurred three

weeks later, after quick decompression following an eight-hour shift at twenty-seven pounds. He returned to the lock on account of severe pains similar to those of the first attack, and improved rapidly. Went out again slowly and was able to return to work the next day. Four weeks later he had the third attack, which came on less than one hour after coming out rapidly from a pressure of twenty-seven pounds. He had to go to a cold room, although according to the rules, a warm one should have been provided. He had pain like that of the previous attacks.

In 1907 he worked for three months at Clinton, Iowa. In the course of the work the pressure was gradually raised to twenty-seven pounds. After coming out from a four-hour shift with wet feet, on account of leaking boots, he was taken in three-quarters of an hour with the same kind of pain as before. He returned to the lock, remained one hour, came out slowly, and was well. He did not return to work there, but in 1909 he worked on the Northwestern Depot, Chicago, under a pressure of about eighteen pounds. He was "blocked" a few times, but had no other trouble.

He now works in open caissons and is in good health, with the exception that the legs are often stiff in damp weather. He never had this trouble before the attack of "bends."

Watch-tick heard at one and one-half inches in the right ear; four inches in the left.

When seen again, June, 1912, he still complained of pain in the knees and ankles in changeable weather, "in the same place where he had the bends." The knee and ankle jerks were sluggish, and both tactile and pain sense seemed to be reduced from the knees down. The patient has seven children, and denies venereal disease.

Dr. Hollis E. Potter made an x-ray examination of the knees. Two inches below the left knee-joint there are changes in the spongy tissue of the tibia in the shape of irregularly branching or stellate islands of sclerosis. Dr. Potter is of the opinion that this appearance is caused by a reconstruction of the bone following an atrophic process. There is also a bulging thickening in the surface of the tibia just below the head of the fibula. The right knee shows no change.

CLASS III. EAR AFFECTIONS.

As stated, 87 of the 161 men gave a history of ear affections, and 65 have more or less impairment of hearing; 33 complained of dizziness. Rupture of the drum, which, according to the large experience of Koch³ and of Chrabrostin,⁴ is rare, was said to have occurred in our Cases III and XIV, related elsewhere in this paper, and in one other case. However, we only have the patient's state-

³ Festschr. Friedr. Wilhelmsinst, Berlin, 1895.

⁴ Official Report on Work under Water to Russian Navy Department, 1882. Cited after Heller, Mager, and Schrötter: Die Luftdruckerkrankungen.

ment that they were so informed by some doctor, who might have drawn the erroneous conclusion that hemorrhage from the meatus indicated rupture of the drum. Such hemorrhage had taken place in a large number of cases.

Eight of the men with more or less marked permanent deafness were referred to Dr. G. W. Boot for otological examination. In every one a diagnosis of labyrinthine deafness was arrived at. In five of these men marked nasal obstruction was present, caused by deflected septum or enlarged turbinates, which furnishes a reason for the liability of these men to be "blocked" on entering the caissons. Four of them state distinctly that the ear symptoms came on after decompression, which harmonizes with the labyrinthine character of the deafness. However, according to Heller, Mager, and Schrötter,⁵ the general experience has been that "decompression is of no importance in caisson workers when the ears are healthy." The presence of nasal obstruction in so many of our men therefore becomes significant, as the ears may have been diseased beforehand, and as such obstruction would render equalization of pressure by means of free passage of air through the Eustachian tubes extremely difficult.

CASE XVI.—Eighteen years ago partly "blocked" on entrance; after decompression pain in ear, vomiting, vertigo, total deafness for a time; persistent tinnitus and partial deafness.

Male, aged thirty-six years. In 1894 he was partly "blocked" on entering a pressure of twenty-seven pounds. Two and a half hours after coming out he was taken with pain in the left ear, vomiting, vertigo, and delirium. He was delirious for several days, during which there was considerable bleeding from the left ear, and later discharge of pus. There was total deafness at first, but soon hearing was partly restored. He has never been in compressed air since then. Left-sided tinnitus has persisted, and he often feels dizzy. Dr. Boot examined him in June, 1912, and reports:

"Whisper in right ear heard at 30 cm.; in left ear loud whisper only heard close to the ear. Bone conduction much shortened. Weber to the left. Low limit: Hears 32 with each ear. C-4 shortened in the left ear. Upper limit: R., 20,000; L., 19,000. Throat normal. Nasal septum deflected to the right. Right tympanic membrane lusterless, position normal. Left retracted, luster good. Irrigation of the right ear with cold water gives rotary and horizontal nystagmus to the left. Irrigation of the left ear with cold water gives rotary and horizontal nystagmus to the right, chiefly rotary. Hearing improved by inflation. Diagnosis: Tubal occlusion; labyrinthine deafness."

No further discussion of the ear findings in these cases will be given here, as Dr. Boot will publish a separate article on this subject in the near future.

⁵ *Loc. cit.*, p. 1003.

PERSISTENT DUCTUS BOTALLI AND ITS DIAGNOSIS BY THE ORTHODIAGRAPH.

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THE diagnosis of congenital cardiac disease is so notoriously uncertain that any aid to its accurate accomplishment is worthy of careful study. This is especially true of the lesion which forms the subject of this paper—patent ductus arteriosus—in view of the fact that clinicians for many years have doubted the possibility of its certain diagnosis *intra vitam*. For this feeling there was ample justification until the study of this condition by the *x*-rays, and especially by the fluoroscope, revealed a pathognomonic change in the configuration of the heart which made it possible to diagnosticate it with reasonable certainty. To understand the significance of this discovery, it is necessary to rehearse briefly the appearance of the normal heart silhouette as revealed by the fluoroscope.

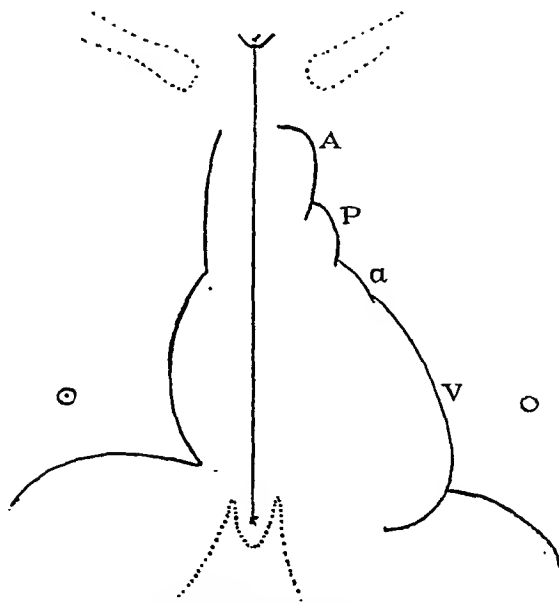


FIG. 1.—Orthodiagram of normal heart, reduced. A, aorta, P, pulmonary artery; α, left auricle; V, left ventricle.

The left side of the heart shadow normally appears as a broken convex curve composed of four elements, as follows (Fig. 1): Beginning from above one sees a large curve due to the arch of

the aorta (*A*); below this and somewhat smaller appears the curve of the pulmonary artery (*P*); below this and but faintly indicated is the left auricular appendage (*a*); and finally is seen the large curve of the left ventricle (*V*). Each of these pulsates, the excursions having different amplitudes. The aorta shows an excursion of moderate extent, the pulmonary artery one of less extent, the auricular appendix usually appears immobile, and finally the larger, wider pulsation of the left ventricle is apparent.

In patent ductus arteriosus the appearance of the heart above described is modified in the following manner: The middle area of the left border of the heart shadow is much enlarged, so that in extreme cases a ball-like prominence here surmounts the heart. The position and pulsation phase of this shadow show it to be that of the pulmonary artery. Moreover, whereas the normal pulmonary artery beats but slightly, and with less vigor than the aorta, in cases of persistent ductus Botalli the pulmonary artery pulsates more powerfully than its neighbor. On watching this shadow one gains the impression that with each systole the pulmonary artery is actively distended by an increased volume of blood.

This observation was made fifteen years ago by Zinn,¹ and has since been verified by De la Camp,² Hochsinger,³ Bittorf,⁴ and others, and recently by Groedel, who has used the orthodiagraph for the diagnosis of the condition. This enlargement of the pulmonary artery is logically explained by the influx of blood into it from two sources: the right ventricle and the ductus arteriosus, leading to its dilatation. The fluoroscopic appearance is correlated with the band of dulness along the left border of the sternum in the three upper interspaces first described by Gerhardt⁵ in 1876, and since then known as Gerhardt's sign. The value to the clinician of this fluoroscopic appearance is heightened when one interrogates the opinions of those who have studied this defect, and realizes how varying are the physical signs which have been pointed out as characteristic of this condition.

Vierort⁶ has formulated the physical signs of patent ductus arteriosus as follows: A murmur which is usually systolic is heard over the pulmonary area; hypertrophy of the right side of the heart; accentuated second pulmonic sound.

Gibson⁷ may be quoted in his own words as follows: "The

¹ Zur Diagnose der Persistenz des Ductus a. Botalli, Berl. klin. Woch., 1898, No. 20, p. 433.

² Congenitale Herzleiden, Die Deutsche Klinik am Eingang des XX Jahrhunderts, p. 108, et seq.; also Berl. klin. Woch., 1903, No. 3, p. 48.

³ Zur Diagnose der Persistenz des Botallischen Ganges und der Erweiterung der Lungenarterie, Wiener Klinik, 1907, p. 311 to 348.

⁴ Ein Fall von offenem Ductus Botalli, Münch. med. Woch., 1903, No. 41.

⁵ Persistenz des Ductus arteriosus Botalli, Jena Zeitsch., 1876, iii, No. 2.

⁶ Nothnagel's System.

⁷ Persistence of the Arterial Duct and its Diagnosis, Edinburgh Med. Jour., 1900, viii, 1.

diagnosis of patent ductus arteriosus may be founded with perfect confidence. The recognition of the lesion may depend on the presence of a few physical signs. . . . Palpation usually reveals a long thrill following the apical impulse and enduring beyond the recoil of the blood on the semilunar cusps, which may be felt during the thrill; percussion may not show any enlargement of the cardiac dulness, while auscultation gives convincing proof of the lesion in a murmur which may be regarded as almost pathognomonic. Beginning directly after the first sound it accompanies the latter part of that sound, occupies the short pause, accompanies the second sound, may be and often is doubled, and finally dies away during the long pause."

Hochsinger,⁸ who has perhaps studied this subject most intensively, has endeavored to unravel its diagnosis in the presence of associated lesions, and insists on the following signs as necessary: (1) Palpable and much accentuated second pulmonic sound. (2) Gerhardt's sign. (3) Thrill felt in the jugulum. (4) Enlarged pulmonary artery in the x-ray picture. (5) Murmur in second left intercostal space, which in infancy is always systolic in uncomplicated cases, but as dilatation of the pulmonary artery develops, may extend into diastole.

Carpenter,⁹ in a study based on extensive clinical material and autopsies, lays stress on the following points in diagnosing patency of the ductus arteriosus: (1) A systolic murmur, loudest over the second left interspace, occasionally transmitted upward and heard in the interscapular region; in adults it is commonly prolonged into diastole, and is of a roaring, rumbling character. In children, on the other hand, this harsh character is lacking, and the prolongation into the diastolic period is of infrequent occurrence. (2) A thrill is not constant; it may be present over the pulmonary area, and when transmitted to the left clavicle is pathognomonic. (3) The second pulmonic sound is usually accentuated, but this sign is not essential to the diagnosis. (4) The presence of Gerhardt's dulness. (5) The x-rays constantly show an enlarged pulmonary artery. (6) The heart is not enlarged to the right.

Groedel,¹⁰ who has studied a series of cases with the orthodiagraph, summarizes his findings as follows: (1) "Of all the congenital affections the persistence of the ductus arteriosus Botalli affords the most typical Röntgen picture. The most evident symptoms are the distention and pulsation of the pulmonary artery and the enlargement of the right ventricle by which a round heart is formed." (2) The heart may be normal in size or enlarged,

⁸ Loc. cit.

⁹ Congenital Heart Affections, *British Jour. Child. Dis.*, 1909, No. 69, vol. vi.

¹⁰ X-ray in Heart Diagnosis, *Interstate Med. Jour.*, June, 1911; also *Deutsch. Arch. f. klin. Med.*, 1911, ciii, 413.

depending on the presence of associated lesions. (3) The murmur may be systolic-diastolic.

Other observers have emphasized the significance of one or another physical sign, thus: Zinn¹¹ dwells on Gerhardt's dulness and absence of cyanosis; Dresler¹² lays stress on the transmission of the murmur to the left carotid; Dogutschagew calls attention to the asymmetry of the pulses; while Francois Frank¹³ believes the audibility of the murmur in the interscapular space is of importance. Recently, E. Goodman¹⁴ has collected all of the reported cases of patent ductus arteriosus, adding to them a carefully observed case of his own. His report covers 34 cases in which the diagnosis was corroborated by autopsy and 37 in which it was made purely on clinical evidence. He has carefully analyzed the various symptoms and signs present in each group of cases, concluding that no one particular physical sign should be considered pathognomonic, but rather that the diagnosis should rest upon the presence of a large number of different signs.

The following 5 cases of patent ductus arteriosus were seen by us during the past year. Four of these cases applied for treatment at one of the children's clinics at Mount Sinai dispensary, the fifth occurred in Mount Sinai Hospital in the medical service of Dr. Alfred Meyer, through whose kindness we are enabled to report it. All these cases were orthodiographed by one of us in the x-ray department of the hospital.

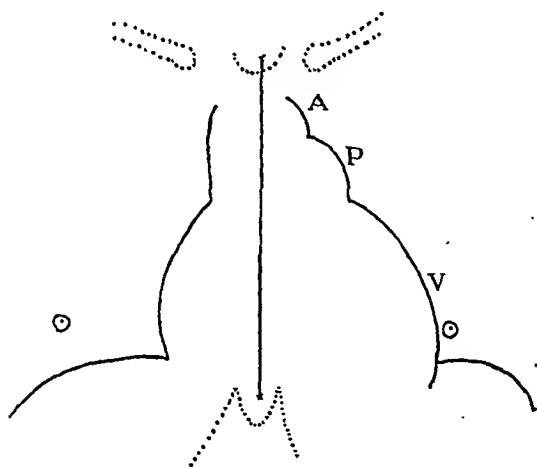


FIG. 2.—Case 1. Transverse diameter, 9 cm.; normal diameter, 8 cm. At P is seen a large, pulsating pulmonary artery. Heart enlarged mainly to right, producing so-called "Kugel-herz" or round heart.

¹¹ *Lac. cit.*

¹² Beitrag zur Diagnose des Ductus a. Botalli, *Jahr. f. Kinderheilk.*, 1902, lvi, 705.

¹³ *Gaz. Hebdomad.*, 1878.

¹⁴ Report of a Case of Patent Ductus Arteriosus Botalli, with a Study of the Cases heretofore Published, *Univ. Penna. Med. Bull.*, 1910-1911, No. 10, p. 509.

CASE I (Fig. 2).—Isidor S., male, aged six years.

History: Normal birth. Not a "blue baby," though fingers have always been somewhat bluish. Pertussis three years ago. No other serious illness.

Present illness dates back four weeks, since when the patient has had slight cough, malaise, and toward evening fever. Has lost considerable weight.

Physical Examination: Undersized, poorly developed boy. Moderate general cyanosis. Marked clubbing of fingers and toes. Lungs show general bronchitis.

Heart: Apex-beat visible and palpable in the fifth space in the nipple-line. Heart borders normal to percussion. There is a loud, rough systolic murmur heard all over the chest, with the maximum intensity over the second left intercostal space close to the sternum. Loud clear ringing second pulmonic sound, which is also distinctly palpable. Pulses equal, regular, of good volume. Heart apparently well compensated.

Urine negative. Von Pirquet reaction strongly positive.

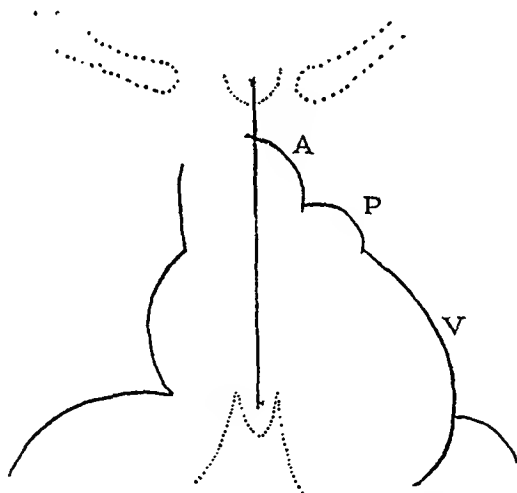


Fig. 3.—Case II. Transverse diameter, 7.5 cm.; normal diameter, 8.4 cm. At P is seen large pulsating pulmonary artery. Heart is not enlarged.

CASE II (Figs. 3 and 4).—Mollie N., female, aged four years.

History: Normal birth. Except for measles at two years of age has always been well. Was brought to the clinic for a slight cough of two weeks' duration. No loss of weight. No fever. No hemoptysis.

Physical Examination: Undersized girl. Good color. No cyanosis or clubbing.

Heart: By percussion enlarged to the right and left: Right border, second space, 2 cm. to right of midline; third space, $2\frac{1}{2}$ cm. to right of midline; fourth space, 3 cm. to right of midline.

Left border: Third space, 4 cm. to left of midline; fourth

space, 5 cm. to left of midline; fifth space, $5\frac{1}{2}$ cm. to left of midline.

In the left second space there is parasternal dulness extending 2 cm. from the midline. Apex impulse diffusely felt in the fourth and fifth spaces in the nipple line. Action regular. Normal rate. Inconstant faint, rough systolic murmur at apex. In the left second space there is a loud rumbling systolic murmur heard during the greater part of the cardiac cycle, transmitted to the vessels of the neck and downward to the third space. It is not heard in the back. Pulmonic second sound slightly accentuated. Faint thrill in the jugulum and over second left interspace close to the sternum. Pulses equal, good quality. Urine negative.



FIG. 4.—Case II. Roentgenogram, showing at *P* prominence of pulmonary artery. Comparison with the orthodiagram (Fig. 3) shows the advantage of the latter in point of clearness. From a study of the Roentgenogram alone a diagnosis in this case would not be possible.

CASE III (Figs. 5 and 6).—Esther G., female, aged four and one-half years.

History: Normal birth. No cyanosis. Measles at two years. Pertussis and varicella at three years. Was brought to the clinic for a slight cough, which has troubled her for two weeks.

Physical Examination: Undersized child. Over left temporal region there is an area of bluish-black discoloration about the size of a silver dollar (Mongolian spot). General color good; no trace of cyanosis. No clubbing of fingers or toes.

Heart: Apex beat not visible; impulse felt in the fourth and fifth spaces in the nipple line. Precussion shows the borders as follows:

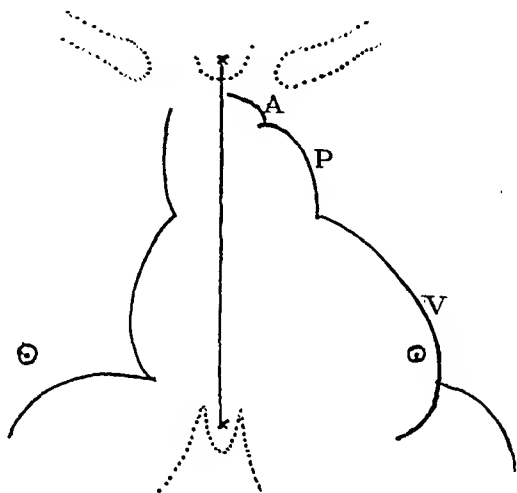


FIG. 5.—Case III. Transverse diameter, 7.7 cm.; normal diameter, 7.9 cm. At *P* is shown a very large pulsating pulmonary artery. Heart appears otherwise normal.

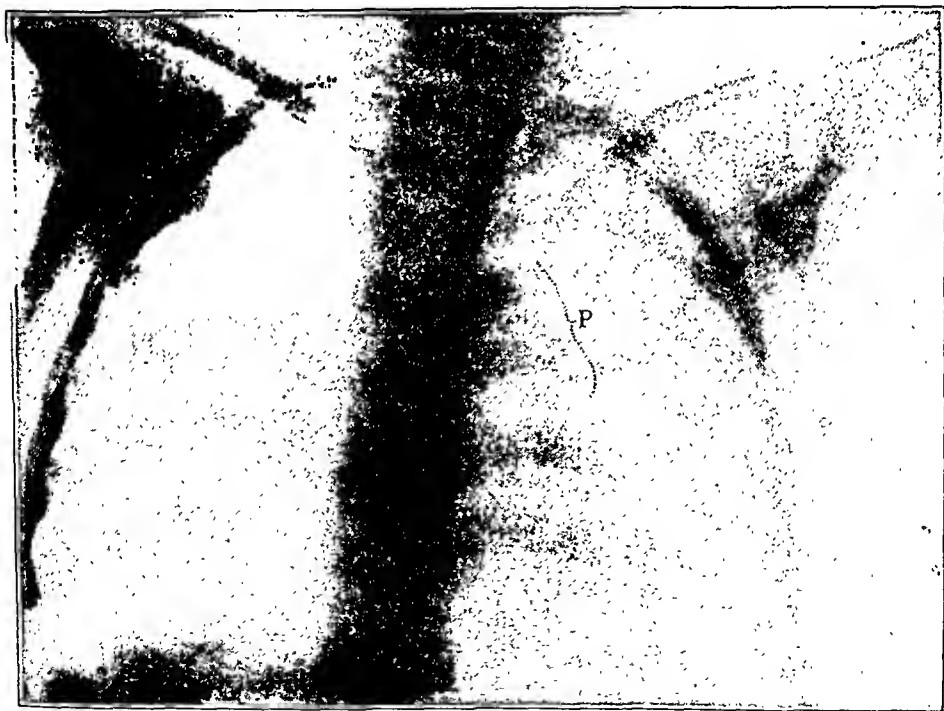


FIG. 6.—Case III. Roentgenogram, showing at *P* a very large pulmonary artery.

Right border, second space, 1 cm. from midline; third space, 1.5 cm. from midline; fourth space 2 cm., from midline.

Left border, second space, 2.5 cm. from midline; third space, 3.5 cm. from midline; fourth space, 5 cm. from midline; fifth space, 7 cm. from midline.

Action regular. Rate normal. First sound at apex is accompanied by a short, rough, systolic murmur transmitted toward the axilla. There is a loud rough, systolic murmur heard best in the second left space, less loud in the third and fourth spaces. It is transmitted to the carotids, and is heard in the left interscapular region. The second pulmonic sound is distinctly loud, but not palpable or ringing. Pulses equal, good quality, regular.

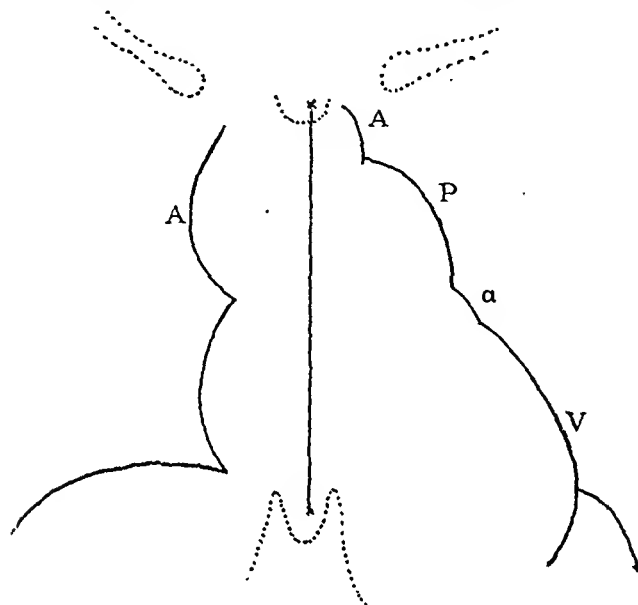


FIG. 7.—Case IV. Transverse diameter, 10.1 cm.; normal diameter, 9.1 cm. At *P* is seen a large pulsating pulmonary artery. Ascending aorta, *A*, is much dilated; enlargement of heart to left.

CASE IV (Fig. 7).—Joe I., male, aged eight and one-half years.

History: Normal birth; no cyanosis. Measles and pertussis in early childhood. For the past year has had headache and occasional vomiting and sticking in the precordium. Night-starts.

Family History: Six children. No cardiac complaints.

Physical Examination: Well nourished. No cyanosis or clubbing. Heart: The right border is 2 cm. to the right of the midline. The left border 9 cm. to the left of the midline. There is a band of dullness to the left of the sternum in the second space. The action is regular and the rate normal. In the second left space there is a rough systolic murmur, transmitted slightly upward. The second pulmonic sound is loud, and is accompanied by a short, rough, diastolic murmur heard also in the third space. There are no murmurs over the aortic area. The first sound at the apex is slightly impure. No thrill. Pulses are equal, regular, not of the water-hammer type. No capillary pulse.

CASE V (Fig. 8).—A. S., male, aged thirty years.

History: Family history negative for tuberculosis and cardiac disease.

Past History: Normal birth. Rheumatism fifteen years ago. For past few months has had a cough; slight fever, and chilly sensations.

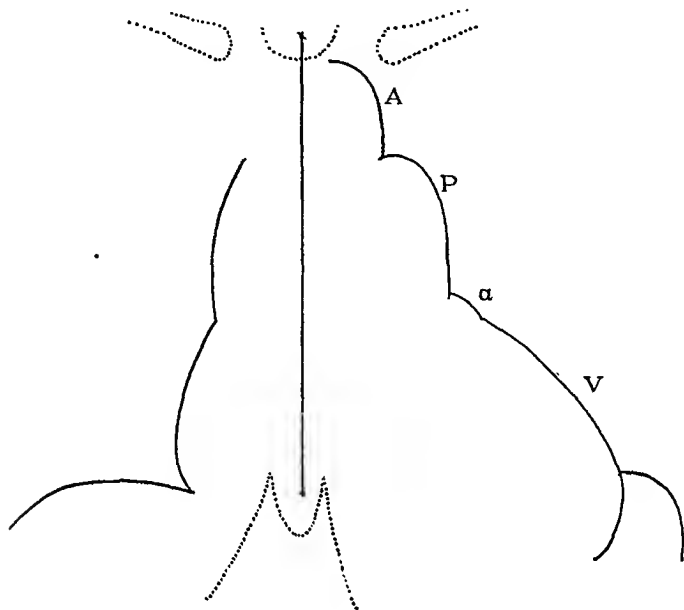


FIG 8.—Case V. Transverse diameter, 13.6 em.; normal diameter, 13.2 em. At *P* is seen a much enlarged and pulsating pulmonary artery.

Present Illness: In hospital at present for mild polyarticular inflammation. At various times while in hospital he developed crops of small subcutaneous nodules, probably tuberculides.

Physical Examination: Well-nourished man. No cyanosis or clubbing. Lungs: Signs of moderately advanced bilateral tuberculosis. Sputum contains tubercle bacilli. Heart: Percussion shows no increase of heart dulness. To the left of the sternum there is dulness in the second space. There is visible pulsation over the pulmonic area. No thrill felt. There is distinct pulsation present in the jugulum. The action is rapid and regular. There is a loud rough systolic murmur best heard over the third left interspace and not transmitted. The second sound over the pulmonic area is accentuated.

To review briefly the salient features of the above 5 cases reference should be made to the table on page 553. It will be seen that though all the cases presented a distinct cardiac lesion, only one of them complained of subjective symptoms. All the hearts were compensated. Cyanosis and clubbing of the fingers were present only once, and 2 of the cases were suffering from pulmonary tuberculosis. A rough basic systolic murmur was uniformly

present. It was best heard over the pulmonic area, and in 1 case extended throughout the cardiac cycle. This murmur was usually transmitted to the neck, and in only 1 case was it heard in the left interscapular region. With one exception the size of the heart as determined by percussion was normal, and in one other case the orthodiagram showed an enlargement to the right. The second pulmonic sound was in all cases distinctly accentuated and of pure quality, and the closure of the pulmonary valves was palpable in one patient. A thrill was found in one case only, and it was faintly felt in the jugulum and over the pulmonic area. Parasternal dulness (Gerhardt's sign) was elicited in 4 of the patients, but was not noted in one case.

There is, therefore, a distinct similarity in the physical signs shown by these 5 cases, and one is further convinced of this by the *x*-ray findings. In 2 of the cases (Nos. 2 and 3) radiographs were made, and the accompanying reproductions show a distinctly prominent shadow in the region of the pulmonary artery (Figs. 4 and 6). It is, however, in the orthodiagraphic pictures (Figs. 2, 3, 5, 7, and 8) that the enlargement of the pulmonic shadow is most beautifully shown. In each picture the bulging of the pulmonary artery (*P*), before referred to, is evident, and is easily seen when compared with the diagram of the normal heart (Fig. 1). On fluoroscopic examination the pulsation of this pulmonic shadow was the dominating feature of each picture.

As regards the size of the hearts, only one case showed enlargement to the right (Fig. 2), and one case showed enlargement to the left (Fig. 7).

The shape of the heart as revealed by the orthodiagraph is also of importance. Three of the 5 cases are of normal shape. Of the 2 others, one has evidence of left ventricle hypertrophy and dilatation; the other shows an enlargement to the right and a rounded shape (Kugelherz), characteristic of right-sided enlargement. These 2 cases differ from the others not only in their fluoroscopic appearance, but also in their physical and clinical manifestations. Examination of Fig. 7 shows a dilated pulsating ascending aorta, with hypertrophy and dilatation of the left ventricle. This is the characteristic appearance found in stenosis of the aortic isthmus, a lesion commonly associated with patent ductus arteriosus, and aortic insufficiency has probably developed. It is incidentally of interest to note that this case with its secondarily acquired lesion is the only one showing any subjective cardiac symptoms. The other case in which there is a variation from the normal configuration is shown in Fig. 2. In this case an associated congenital lesion had been suspected, owing to the marked clubbing and cyanosis it presented. According to Hochsinger there is a probability of combination with pulmonary stenosis, when there is marked hypertrophy of the right ventricle and a high grade of cyanosis in the early years of life.

TABLE SHOWING SIGNS AND SYMPTOMS OF THE FIVE CASES REPORTED.

Case No.	Age.	Sex.	Subjective symptoms.	Clubbing of fingers.	Cyanosis.	Size of heart.	Systolic Murmur.	Transmission of murmur.	Other murmurs.	Character of second pulmonic sound	Thrill.	Gerhardt's sign.	Frank's sign.
I	6 years	M.	None	Marked	Marked	+ to right; "Kugel" shape	All over chest, loudest over pulmonic area	Over entire chest	None	Loud ringing, palpable	None	Not elicited.	Not elicited.
II	4 years	F.	None	None.	None	Normal	Rumbling over greater part of cardiac cycle. Loudest over second left space	To neck and downward to third space	Faint rough systolic at apex	Slightly accentuated	Faint, in jugulum and over second space	Present	Absent.
III	4½ years	F.	None	None	None	Normal	Rough. Over second left space	To carotids	At apex a short systolic transmitted to axilla	Accentuated.	None	Present	Present.
IV	8½ years	M.	Slight precordial pain. Sleep-starts	None	None	+ to left; "aortic" shape	Rough over second left space	Slightly upward, but not to neck vessels	Soft diastolic in second left space transmitted to third space	Loud	None	Present	Absent.
V	30 years	M.	None	None	None	Normal	Rough over third left space	None	None	Loud and accentuated	None	Present	Not elicited.

From the study of our orthodiagrams, therefore, it appears that in pure patent ductus arteriosus one need not expect enlargement of the heart or alteration of its shape, and that the presence of these changes suggests an associated or complicating lesion.

DIFFERENTIAL DIAGNOSIS. One lesion with which patent ductus arteriosus may be confused is pulmonary stenosis, inasmuch as the physical signs are much alike. Hochsinger insists that the diagnosis of patent ductus Botalli should not be made in the absence of a much accentuated second pulmonic sound. A second pulmonic sound of normal intensity, or one which is impure, at once suggests diseased pulmonic valve cusps which do not vibrate in response to the increased pressure in the artery—most probably pulmonic stenosis. It appears that in pulmonic stenosis the pulmonary artery may be congenitally hypoplastic, causing it to dilate under the influence of pressure, so that on viewing it with the *x*-rays it appears enlarged. This was the case in the patient reported by Arnheim,¹⁵ in which a diagnosis of patent ductus arteriosus was made, in which, however, at autopsy an extreme pulmonic stenosis was revealed. Hochsinger, in discussing this case shows that there was absent pulmonic second sound, which should have thrown out the diagnosis of patent ductus arteriosus. It is of interest to note that in his article Arnheim makes no mention of having watched the heart in action, confining himself to an *x*-ray plate. It seems highly improbable that the large pulmonary artery he pictures would have shown the wide pulsation as we have seen in all of our cases. In the presence of extreme narrowing of the pulmonary artery one would not expect a marked systolic expansion of the shadow, and we believe that had Arnheim fluoroscoped his case the error in diagnosis might have been avoided.

In Burke's 3 cases¹⁶ of pulmonic stenosis with autopsy, in which during life a patent ductus was diagnosticated because of accentuated second pulmonic, there is no record of fluoroscopic examination; so that this observer did not avail himself of perhaps the only means of diagnosis which would have been differential.

There is one other condition in which the pulmonary artery may be much enlarged—namely, mitral disease. We have, however, been able to convince ourselves by frequent fluoroscopy of these cases that the pulmonary artery in this condition while enlarged, pulsates little if at all. In this connection the case of patent ductus arteriosus reported by Kate Campbell Mead¹⁷ is of interest. In this case the diagnosis of patent ductus was made by Dr. Thayer, to whom the patient had been referred. Two years later a laryngeal par-

¹⁵ Persistenz des Ductus Botalli, Berl. klin. Woch., 1903, No. 27, and 1905, No. 8, p. 206.

¹⁶ Zeitschr. f. Heilkunde, 1902.

¹⁷ Persistent Patency of the Ductus Arteriosus, etc., Jour. Amer. Med. Assoc., December 24, 1910.

alysis appeared and the patient was x-rayed. The x-ray picture shows a cap-like prominence in the pulmonic region, which, however, is interpreted in the radiographer's report as the shadow "due to an hypertrophied and dilated left auricle, secondary to an insufficient mitral valve." No mention is made of fluoroscopy, and it is certain that observation of this case by means of the fluoroscope would also have shown the characteristic silhouette and pulsation.

We believe that a comparison of the clinical findings and the fluoroscopic appearance of our cases with those reported in the literature corroborated by autopsy fully justifies our diagnosis of patency of the ductus arteriosus.¹⁸ Furthermore, we are impressed by the importance and value of fluoroscopic examination, and believe that diagnosis is distinctly aided by careful observation of the heart in action.

We wish to express our thanks to Dr. Jaches, of the x-ray department of Mt. Sinai Hospital, for courtesies extended during the course of this work.

A STUDY OF EMPYEMA, WITH SPECIAL REFERENCE TO THE FEASIBILITY AND IMPORTANCE OF DEPENDENT DRAINAGE.

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(Concluded from March, 1913, p. 422.)

MASSIVE (PARIETAL) EMPYEMAS

CASE I.—On February 13, 1906, I operated for the late Dr. Southwick on a girl, aged seven years, who had been rapidly accumulating a pleural effusion on the left side, soon after the crisis of a double pneumonia. The dullness was general and the dyspnea marked. Temperature, 101° F. Paracentesis was done in the seventh interspace in the scapular line for the relief of the dyspnea and for diagnosis. About a quart of purulent fluid was

¹⁸ In another case to be reported by Dr. M. Manges, in whose service it occurred, the diagnosis of patent ductus arteriosus was made. This case was orthodiagraphed by one of us (H. W.), and the fluoroscopic appearance was found to be identical with that of the cases described above. The patient died of carcinoma a few weeks later, and at autopsy patency of the ductus arteriosus was found.

drawn. Two days later about $1\frac{1}{2}$ inches of tenth rib was resected in the scapular line and more pus evacuated. The index finger introduced through the wound could not touch any part of the lung except a substance with a velvety feel in the direction of the spine. This was probably collapsed lung. When the finger was turned downward it could easily feel the bottom of the pleural cavity and the twelfth rib and came against the diaphragm. The opening was extended across the interspace to the top of the eleventh rib. Two large drainage tubes were introduced about 5 inches and sutured to the edges of the wound and the usual large dressing was applied. Three days later the tubes were removed and the finger again introduced. It could now touch lung which was evidently reëxpanding. As the opening was fairly large a portion of the lung could be seen. The patient was much improved. Temperature, 99° F. About 1 inch of each tube removed before replacing them. Eight days later and eleven days after the operation, when I saw her again, the finger recognized a decided gain in expansion of the lung. As on the last visit it passed into the fissure between the two lobes, which now had come closer together, and the external surface of the lung closer to the chest wall. One week later the finger failed to recognize any gain in expansion, and forced respiratory apparatus with two bottles was advised. In the following two weeks only slight gain was evident. On April 15, the tubes were removed and two weeks later the sinus had closed.

CASE II.—Man, aged thirty years. Right-sided croupous pneumonia began March 13, 1906, when Dr. Winslow Drummond was called. Had his crisis in nine days, which was followed by a short period of undisturbed convalescence, and this in turn by an increasing disturbance on the same side of the chest. Pleural effusion recognized March 26. A few days later aspiration tried at several points without obtaining pus or other fluid. I saw the patient first on April 5 and by that time the dullness extended from the bottom of the chest upward to the third rib anteriorly and the spine of the scapula posteriorly. Breath sounds over the dull area were absent or indistinct. Patient admitted to the University Hospital, in the service of Professor J. William White, April 6. On the same day a large veterinary hypodermic needle introduced in the ninth interspace, with an upward slant to avoid the diaphragm, and a few drops of thick pus obtained. On the following day about 2 inches of the tenth rib removed and empyema opened, a large quantity of thick pus escaping. A finger introduced felt a small portion of collapsed lung. Two large rubber drainage-tubes introduced about 3 inches and sutured to margins of wound, a safety-pin being passed through each for further safety against falling in of the tubes. The space around and between the tubes was packed with gauze strips. Temperature dropped to normal in a few days and the patient's general condition rapidly improved

Air could be heard sucking through the opening until the end of the sixth week. The last tube was removed about the end of the eighth week, and two weeks later the sinus was closed. As it seemed that the large opening necessitated by the two tubes allowed too free an entrance of air I concluded to use only one tube after this.

CASE III.—Boy, aged four years. Referred by Dr. B. F. Wentz. Admitted to the University Hospital, in the service of Professor J. William White, November 10, 1908. On the preceding day Dr. Wentz had found pus with the needle. The boy had been taken with left-sided croupous pneumonia about three weeks before, and had his crisis on the tenth day. He did not recover completely, and during the last few days was feeling much weaker than since the crisis had occurred. The dulness covered almost the whole left side of the chest, but there was slight resonance over the upper part of the scapula. On the day of admission, with the patient in the prone position, suggested by Elsberg, I excised about $\frac{3}{4}$ inch of the eleventh rib near the spine, in the manner already described. On introducing my finger into the cavity I detected an apparently uniform layer of soft fibrin, $\frac{3}{4}$ to 1 inch thick, covering the pleural surfaces, parietal and diaphragmatic, as far as the finger could reach. A small portion of it was wiped off with the finger and removed. No traces of this fibrin were found later in the dressings. An attempt was made at one time to employ negative tension drainage, with the method described by Schley, but a sudden rise of the temperature and illness of the patient caused me to give it up very soon. The patient was discharged from the hospital, with the tube removed, on December 6. Dr. Wentz reported the sinus closed December 14, thirty-four days after the operation.

CASE IV.—Boy, aged seven years, under the care of Dr. W. Drummond. Had severe erysipelas of the face and neck at nineteen months and a bilateral bronchopneumonia at five years of age. Since then has been strong and healthy. On February 12, 1909, was taken ill with influenza. Four days later had recovered sufficiently to return to school. On the following day, however, he was seized with a severe pain on the left side of the chest. On February 19, his temperature was 101° ; pulse, 98; respiration, 42, and croupous pneumonia was diagnosed. Two days later the temperature had reached $105\frac{2}{5}^{\circ}$ F., and the boy seemed septic, so that Dr. Drummond began to suspect an empyema and tried a small hypodermic needle without obtaining pus. On February 27, Dr. J. H. McKee was called in consultation, concurred in the diagnosis of empyema, and obtained a large quantity of pus by aspiration. On the following day, at the child's home, I excised about an inch of the eleventh rib near the spine (Fig. 1), with the patient in the prone position. I happened to look at a clock as

I was about to make the stab wound for the introduction of the exploratory probe and I concluded to time the operation. When the tube was in and the dressing was being applied from four to five minutes had elapsed. The temperature reached normal on the third day after operation. On the sixteenth day it rose suddenly to $102\frac{3}{8}^{\circ}$ and the patient looked ill. The tube was removed and a plug of fibrin washed out when it was replaced. On the following day the temperature rose again, but after that there was no further trouble. The sinus was not closed until the ninth week, and in this case the sucking in of air on inspiration was heard until about two weeks before the sinus closed.

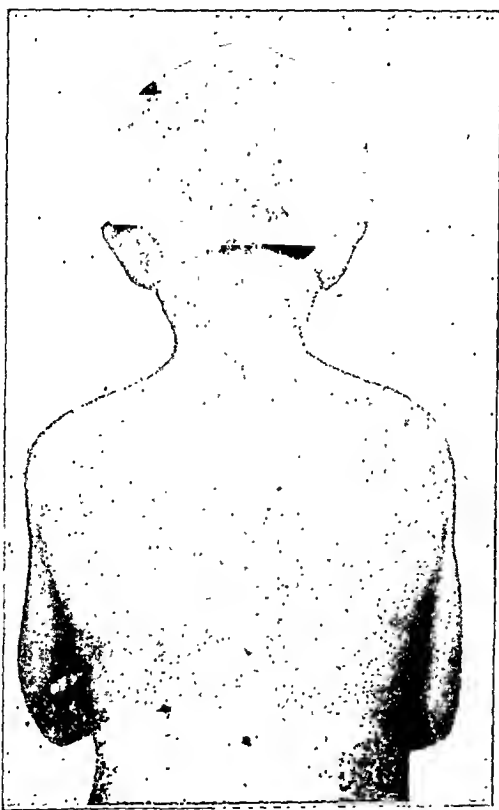


FIG. 1.—Scar at bottom of left side of thorax, posteriorly, after drainage of a massive empyema by excision of small portion of eleventh rib. Inferior angle of scapula normally is opposite seventh intercostal space.

CASE V.—Boy, aged eight years, under the care of Dr. C. L. Felt. Was taken with right-sided pneumonia October 17, 1910. Had his crisis in the usual time, but did not fully recover afterward. Dr. J. H. McKee was called in consultation and confirmed the diagnosis of empyema. On November 6, at the patient's home, I excised a small portion of the eleventh rib, as in the preceding cases. A large quantity of pus was evacuated and a half-inch

rubber drainage-tube introduced and fixed to the margins of the wound. I saw the patient only a few times after the operation, Dr. Felt taking charge of the after-treatment. He reported the sinus closed January 3, 1911, about eight weeks after the operation.

SMALL (INTERLOBAR?) EMPYEMAS.

CASE VI.—This case was reported in conjunction with Dr. J. H. McKee before the Philadelphia Pediatric Society in May, 1906. The patient was under the care of Dr. McKee, who made the diagnosis and located the pus collection. The following is the brief report of the case which I made¹ and the reference to the condition as a "localized or encysted" empyema was made before I had concluded that practically all acute empyemas are localized or encysted. "The opening in the chest wall, made by a resection of about 1 inch of the sixth rib in the midaxilla on the left side, led directly into the cavity. That the empyema was a localized or encysted one was shown by the fact that the lung was adherent to the parietal pleura in the circumference of the empyema, which was demonstrated by the exploring finger. That the pus collection was in the fissure was evident from the depth of the cavity, which was approximately in the normal situation of the fissure dividing the two lobes of the left lung, and from the fact that the finger came directly upon the heart, covered by the pericardium. Drainage was provided by two good-sized rubber tubes, introduced in the direction of the spine for about 5 inches. These were gradually shortened and healing was completed in five weeks. At the time of the operation the finger entered a roomy cavity, the walls of which were apparently under the influence of external atmospheric pressure. Soon afterward it could be determined through the wound by the eye and finger that the cavity was becoming filled by the expansion of the collapsed portion of the lung, this being aided by coughing and forced respiratory exercises."

CASE VII.—Boy, aged two years, under the care of Dr. W. Drummond. Had apparently recovered from right-sided croupous pneumonia, which developed at the end of a three months' illness, including repeated "colds" and a glandular abscess of the neck. He did not remain well after the crisis, and on suspecting an empyema, Dr. Drummond called Dr. J. H. McKee in consultation on February 7, 1908. While dulness was found over the greater part of the left side of the chest it was most marked in the midaxillary region between the sixth and ninth ribs. Aspiration in the seventh interspace gave no pus, and it was repeated in the eighth interspace. No pus appeared on this trial until the needle was with-

¹ International Clinics, 1906, cxi, 159

drawn, when immediately the inside of the bottle was spattered with pus spots, a small quantity appearing at the site of the puncture. On the following day, under chloroform administered by Dr. A. G. Tinney, and with the assistance of Dr. Drummond, I first made a stab wound with a narrow bistoury at the site of the aspiration puncture. A probe with the end bent slightly was introduced, but it could not be moved about freely inside the chest, and its end could not be turned downward. About an inch of the rib below was excised. The pleura was broken through by a grooved director, but only a small quantity of pus escaped. This opening was enlarged and a finger introduced, which found itself in a very small space, with the drainage opening at its lowest limit and the lung adherent to the chest wall all around the cavity. A drainage-tube with a half-inch lumen was introduced, sutured to the margins of the wound, and the dressing applied. The quantity of pus which escaped was small and about two tablespoonfuls of a fibrinous material escaped also. After the operation the child did not improve rapidly and continued to cough considerably, the temperature retaining the same septic type as before the operation. February 15 it was noted that he seemed to cough up a considerable quantity of fluid, which could not be inspected because it was immediately swallowed. It may have been the result of the breaking into a bronchus of a second pus collection, as he improved after this for a short time. February 24, the patient had been worse for a few days, and an examination showed an area of dulness just anterior to the upper part of the axilla. Under ether anesthesia aspiration was tried here, but no pus was obtained. The finger was then introduced into the drainage opening, but found itself in the same circumscribed cavity as in the first operation, and brought out a considerable amount of the same fibrinous material as escaped at the first operation. On February 28, on account of the continued sepsis, the tube was removed and the cavity packed with iodoform gauze, but this was stopped and the tube reintroduced in a few days. The area of dulness above persisted, and on account of the continued symptoms of sepsis it was thought that there must be a second pus collection, indicating further operation. Dr. McKee was again called in, but advised against operation. The child was slowly improving, although the temperature still continued to be irregular and about as high as before the operation. Although the cavity was a small one from the beginning, on account of the septic character of the temperature it was thought advisable to allow the tube to remain. On April 24, it was concluded to remove the tube, regardless of the temperature. A few days later the temperature came down to normal and in about ten days the sinus was closed. The patient has continued well ever since and at the present time is in perfect health.

CASE VIII.—Girl, aged eleven years, a private patient in the Germantown Hospital, under the care of Dr. Perry Cummings, who had called in consultation Dr. J. H. McKee. The patient had had right-sided pneumonia and the temperature had fallen by crisis, but had remained normal only a few days. When I first saw her, January 15, 1910, the relapse had lasted about a week, the temperature rising each afternoon to 104° and 105° F., and falling in the morning to about normal. The pulse remained at about 100 to 110 and the respiration at about 40. There was a localized area of dullness, reaching from about the third interspace above to the liver dullness below, and from the sternum to the anterior axillary line. About four days before a hollow needle had been introduced in this dull area, in the third and fourth interspaces, without obtaining pus. It was thought that the needle had not passed into lung tissue. Air had rushed into the chest through the needle, indicating that the visceral and parietal pleuræ were not adherent to each other in the dull area. An x-ray taken seemed to show a small empyema nearer the posterior than the anterior surface of the lung. After a consultation it was concluded that a pus collection was present and that the lung should be exposed for further exploration and the evacuation of a pus collection, if found. On the following day, January 16, the patient was given chloroform by Dr. McKee, and I exposed and removed subperiosteally about $1\frac{1}{2}$ inches of the fourth rib and cartilage. The pleura was then carefully opened after it was picked up by forceps. The lung was adherent to the parietal pleura by delicate adhesions. While separating these in the effort to locate the horizontal fissure of the lung the air began to enter the pleural cavity and the lung slowly to collapse. The lung was quickly grasped with a double tenaculum and drawn into the wound to plug it against the further entrance of air, and the lung was sutured to the circumference of the wound margins to permanently shut off the pleural cavity. A veterinary hypodermic needle was then introduced nearly its whole length into the lung four times in various directions, the piston being withdrawn each time. The results were unsatisfactory, only a small quantity of fluid being withdrawn each time, and that so mixed with blood that its significance could not be determined. The last puncture was made with a slight upward slant of the needle, and after removing it and expelling its contents into a basin it was observed that there were two small white spots in the fluid withdrawn. It was concluded that these showed the presence of pus. The actual cautery was then passed about $1\frac{1}{2}$ inches into the lung in the direction of the last puncture, but no escape of pus followed it. A closed hemostatic forceps was then introduced into the lung opening, forced about an inch deeper, and the blades opened slightly. There immediately followed a gush of fluid, the nature of which could not be

determined because of the blood present. The fluid flowed too easily to be pure pus, but it was not blood because the flow ceased immediately. None escaped into a bronchus. The quantity could not be determined, but according to my judgment there were about 2 ounces. The finger passed into the lung wound found what seemed to be a small cavity, with smooth walls which contrasted with the rougher surfaces of the rest of the wound. During the manipulations with the finger, which were gentle, air was heard entering the thoracic cavity and was evidently passing through the lung wound. It is likely that the collection of fluid was in a fissure and that the finger had broken down the circumscribing adhesions in it, so that the pleural cavity was again opened to the outside air through the lung wound. A strip of gauze was immediately packed into the lung wound, shutting off the new opening into the pleural cavity, and the whole wound was thus tightly packed to the skin surface. The skin wound was partly sutured, a dressing applied and held in place by a bandage. The patient was returned to bed in good condition. The external dressing was changed daily, but the packing in the lung wound was allowed to remain until the sixth day, when it was removed under nitrous oxide anesthesia. A rubber tube was then introduced and packed around with gauze, but the tube was removed on the following day and was not replaced afterward, only light gauze packing being employed. Soon after this the packing was done away with entirely, the gauze being merely laid over the wound. The temperature fell to normal on the day after the operation and remained practically so during the convalescence, the wound being almost completely closed on February 14. The patient has since done very well and is now in good health.

CASE IX.—Girl, aged four years. Referred by Dr. B. F. Wentz. Right-sided pneumonia began March 27, 1910, and crisis occurred April 9. The convalescence progressed favorably four or five days, when the patient began to get worse, and there was detected some dulness and other signs of a pleural effusion, including fever and cough. May 18, the dulness reached as high as the third rib anteriorly. Aspiration was done in the seventh interspace in the midaxillary line, but only about 2 ounces of pus were obtained. The patient was admitted to the University Hospital May 19, in the service of Professor J. William White, and operation was performed on the same day. The exploratory probe introduced through the preliminary stab wound was too flexible to serve the purpose well but seemed to reach the eleventh interspace near the spine, although it was recognized that its bent end could not be felt under the eleventh interspace as well as in the preceding large empyemas. The eleventh rib was exposed and a small portion excised. The probe did not push easily through the pleura from the inside as usual, and the pleura was picked up with two

forceps, as in opening the peritoneum, and was carefully incised. This exposed muscle fibers, which were evidently of the diaphragm. A grooved director was then substituted for the probe, and was pushed from within out through the lower opening by keeping it close to the chest wall. No pus appeared. The lower opening was then closed by sutures, a small drain being left in the lower angle. The ninth rib was then exposed and about 1 inch excised. The pleura was opened and a finger introduced, which found a small collection of pus, the escape of which was not accompanied by the usual inrush of air. Percussion showed that the dulness extended as high as before. A veterinary hypodermic needle introduced posteriorly in the seventh interspace withdrew pus. As this puncture was within the reach of the finger from the opening made by the excision of the ninth rib, the finger was introduced in the latter and by keeping it close to the chest wall it was passed upward toward the site of the last puncture when a freer escape of pus occurred than before and air was heard sucking into the chest on inspiration. The quantity of pus escaping, however, was not free enough to indicate the presence of the usual massive type of empyema. A drainage-tube about a half-inch in diameter was introduced and sutured to the margins of the wound, a safety-pin being passed through the tube for added safety. The tube was removed June 6. The patient had left the hospital at the end of the third week with the tube in. The sinus closed during the last week in June, five or six weeks after the operation. The facts that the pus did not extend to the bottom of the pleural cavity and the quantity of pus present was only moderate in amount, together with the fact that it did not escape easily at first through the second opening, suggests the possibility or probability of an interlobar empyema in this case.

SUMMARY. Our knowledge of the mechanical and pathological conditions existing in connection with empyemas has made little progress from observations made at operations or even autopsies. A formalin-hardened cadaver specimen of an empyema undisturbed by an opening during life is difficult to obtain, and therefore rare. For this reason such a specimen affords a particularly valuable opportunity for study. From a study of such a specimen and a small number of clinical cases the writer draws a few inferences which are at variance with the generally accepted views. They are as follows: We have not properly appreciated the extent and the nature of the adhesion formation developing in connection with empyemas, especially the acute variety. The massive parietal type extends usually to the bottom of the normal pleural cavity, and is not unencysted or general, but completely walled off above from the rest of the pleural cavity by adhesions. This explains the slight movability of the dulness on percussion, after changing the position of the patient, as well as the fact that the upper level

of the dulness is not in a straight line as it should be if the fluid was unencysted and free to seek its own level. Skoda's resonance may not be due to relaxation of the lung above the pus, but to the fact that the functioning portion of the lung is doing compensatory work.

The probability is that adhesions between the lung and chest wall will not offer a serious obstacle to the reëxpansion of the lung, because they develop between parts normally in contact. The fact that a double empyema can be safely opened on both sides at the same operation is to be explained by the fact that the air admitted does not produce a total double pneumothorax, since it enters on each side only the firmly walled-off empyemic cavity. Total collapse of the lung is prevented by the firm adhesions which protected the lung against the pus pressure before the drainage opening was made. There is no sudden or dangerous change of pressure on the thoracic organs from the usual rapid evacuation of the pus, but a gradual substitution of the pus by air, which has a pressure of 15 pounds to the square inch.

The so-called encysted or localized empyemas are small, probably because they develop in the fissures of the lung or between the lung and diaphragm, and therefore because of the difficulty with which the pus is diffused in these situations.

The most important factor in preventing the obliteration of the empyemic cavity and closure of the sinus is the pressure of the air admitted through the drainage opening into the empyemic portion of the pleural cavity, where it neutralizes the expanding effect of the air coming through the trachea. Murphy overcomes this completely by aspirating the pus and injecting a formalin-glycerin solution, but his method has not yet received general approval. The drainage methods still prevail. The ideal drainage method is that based upon the suction or siphon principle. Its chief objection is that the devices in use for applying it generally leak air around the tube. We have not yet determined how rapidly an empyemic cavity, which is an abscess, may be permitted to close.

The size of the drainage opening has an important bearing upon the later expansion of the lung. The lung probably cannot expand until the entrance of air through the drainage opening is so diminished by contraction of the opening and blockage of the space in and around the tube by the escaping pus, that with absorption of the air already in the cavity there is developed a negative tension external to the lung sufficient to permit the normal internal pressure coming through the trachea to become greater than the external pressure. For this reason we cannot safely employ in empyemas the large drainage opening as in ordinary abscesses. The effect of the large opening in empyemas is shown after the Estlander operation by the permanent non-expansion of a considerable portion of the affected lung. An opening through the eleventh

rib or interspace of a given size will drain more perfectly than one at the usual level, and will better prevent the entrance of air, since the pus will be constantly escaping and tending to fill the space in and around the tube. There will be little or no danger of the drainage-tube falling into the empyemic cavity, since it must travel against gravity to do so, and if this accident happened the tube probably could easily be reached and removed with a forceps, because gravity would prevent it from moving away from the opening. In some cases the much-thickened pleura is the result probably of the organization of layers of fibrin deposited in the acute stage.

Of the five massive empyemas treated with dependent drainage it may be said that the time necessary for a cure was less in all than the average determined by Schädler, fourteen and one-half weeks, or the average in Fraley's cases, ninety days, and therefore there were no persistent sinuses. In the 9 cases there were no deaths. The method deserves further trial and study.

THE EFFECTS OF EXPOSURE TO INTENSE HEAT ON THE WORKING ORGANISM.¹

BY CHARLES N. FISKE, M.D.,

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THE navy has been consulted in the matter of affections caused by heat and other attending conditions of the atmosphere in which its men work, because this class of disability has attracted attention in the public press and occasional medical reports, either in time of war or in the course of cruises in which the reading public is more or less interested, by reason of prostrations and deaths being noted in published dispatches.

The accompanying statistical table, which records but twenty deaths and thirty-three invalidings from the service on account of heat-stroke during the last thirty-five years, and the damage curve would indicate that heat prostration has been of comparatively little importance to the service as a whole; however, from the excerpts from sanitary reports of naval medical officers to follow and the fact that considerable numbers of cases have on occasion jeopardized the strategic or diplomatic mission of a particular warship, the deep concern of the immediate hygienist will appear to be justified.

¹ Read in Section IV, XVth International Congress on Hygiene and Demography, Washington, D. C., September 24, 1912.

Heat prostrations were coeval with the "new navy" of the last quarter century, which found its beginning in the famous "white squadron;" correspondingly as that early class of all steam-propelled cruisers and gunboats has been retired, and its lessons in sanitation, and notably in ventilation, have been used profitably in the design and equipment of all but the earliest class of battleships and armored cruisers, the factor of heat-stroke in the navy has assumed relatively a low value during the last few years.

Naval hygienists, who have agitated changes in construction, arrangement, and ventilation of ships will represent that the service has largely solved the problem, while other observers will, with perhaps equally good reason, maintain that the difficulty has solved itself on account of smaller boilers and more economical leads of steam pipes and arrangements of pumps, etc., in the engine rooms of large ships. The latter view, however, is refuted by the still lower location of dynamo and steering engine compartments, and in the main it will be evident that improved facilities for ventilation, whether natural or artificial, have achieved the subsidence of heat prostration. It is only when a radically new type of ship is placed in service that faulty and inadequate ventilation any longer occasions suffering and disability from undue atmospheric heat and humidity, as has been recently shown to occur on the first ships of the *Dreadnaught* type.

At their worst, heat affections have developed only on isolated occasions, and then only on comparatively few ships, and doubtless many cases have been so trivial that they have hardly been recognized as of such a nature in the absence of severe cases.

This statement will prepare the physiologists and pathologists who look for some apology or explanation for the naval surgeons not making more definite contributions and exact observations relating to the fairly typical cases of heat exhaustion that occur in the service. It is perhaps thought that with his training, time, equipment, and opportunity to study the condition at its inception, something more than a mere compilation of general data should be available from the reports of naval surgeons for this paper. Such versatility, however, as the wide range of duties demands of naval medical officers, together with the lack of experience and apparatus to make the precise observations which would enable physiologic study to withstand criticism, and the uncertainty of having the cases, which nearly always occur under the unusual and unanticipated conditions on a ship in the tropics, remote from laboratories, as well as the fact that these occasions are likely to find the doctor most busy, preclude the contributions for which we all seek, and which should be more practicable near steel mills, for instance, where cases frequently may be expected and where provision can be made for such study.

The perusal of the literature of disorders attributed to heat

tends to confuse the student first as to nomenclature and terminology and almost hopelessly as to etiology. Within the naval reports comparatively few titles have been used, probably fewer than if more had been available on the printed classification, and save for the quotations from the text of the reports themselves, little dependence can be had upon just what train of symptoms a title was used to cover some fifteen years ago when heat affections were most prevalent in the navy. For these reasons I have combined in the table all heat cases without regard to prevailing nosology.

One of the earliest references to heat prostration in the fire rooms of ships published by an American naval surgeon is the following by Medical Inspector A. L. Gihon, in his *Naval Hygiene*, of 1872:

"The symptoms of insolation often occur among men not exposed to the direct rays of the sun—in the fire room of steamers, on board the monitor class of armored vessels, in small, ill-ventilated cells. Dr. Kitchen informed me that while surgeon of the monitor *Dictator* it was common for men to be brought to him for treatment with coma, stertorous breathing, great heat of skin, full, quick pulse, and often convulsions. The cause was manifestly enough the exhausting labors of a watch in the fire room, where the temperature averaged 145°, and where the ventilation was exceedingly defective, air that had been already respired being repeatedly returned. Maclean states that 'insolation has frequently been observed on board ship, but almost always under conditions similar to those in barracks—that is, where overcrowding and impure air are added to the influence of excessive heat. Insolation is not uncommon on board the mail steamers in the Red Sea in the months of August and September; it has been observed that most of the cases occurred while the sufferers were in the horizontal position in their ill-ventilated cabins,' and he quotes the following: 'Assuredly,' says Dr. Butler, surgeon of the third cavalry, 'those barracks most crowded, least ventilated, and worst provided with punkahs and other appliances to moderate excessive heat, furnished the greatest number of fatal cases.' Surgeon Longmore, of the nineteenth regiment, notes that one-third of his cases and nearly half the deaths occurred in one company of the regiment quartered in the barrack, which was manifestly the worst conditioned as to ventilation, and, indeed, in every sanitary requirement. M. Bassier, a surgeon in the French navy, reports that the man-of-war brig *Le Lynx*, cruising off Cadiz, in the month of August, had eighteen cases of insolation out of a crew of seventy-eight men. The heat was excessive (91° to 95°), and much aggravated by calms. The ship was overcrowded, offering little space for the berthing of the crew. M. Boudin quotes the case of the French man-of-war *Duquesne*, which, while at Rio de Janeiro, had a hundred cases of insolation, out of a crew of six hundred men.

Most of the men were attacked not when exposed to the direct heat of the sun, but at night when in the recumbent position—that is, when breathing not only a hot and suffocating, but also an impure air.”

The works of Surgeon Joseph Wilson, U. S. N., 1870; Medical Directors T. J. Turner, 1879, and A. Gorgas, 1897, and Medical Inspector H. G. Beyer, 1908, include but passing references to heat affections.

Medical Inspector J. D. Gatewood, in his *Naval Hygiene*, 1909, writes:

“About 90 per cent. of all troubles ascribed to heat come from a part of the service—the engineer force in cruising ships serving under conditions that put a large load on the kidneys while depriving them of the fluid necessary to flush themselves properly. The result is a great concentration of irritating urine, and perhaps even anuria if, while the body is bathed in warm sweat, there is a sudden checking of perspiration and rapid chilling of bodies under ventilators or fans. . . . If during the year 1905 all the firemen and coal-passers had been at sea the entire time, there would have been about 200 admissions for heat troubles from each 1000 firemen and coal-passers so employed, and in the year 1899, about 400, *other conditions remaining the same*.

“The intensity has relation, however, to atmospheric conditions while underway and to the course of the ship in relation to wind, high outside temperature, with high relative humidity, and relative state of calm producing the maximum result. The hearts and kidneys and stamina of men, if much speed is maintained, are then greatly tried, especially if new men, some perhaps not well selected, are working as coal-passers. It would therefore seem that, in a general way, tropical cruising, especially in our summer months, and an increasing percentage of recruits in the engineer force tend to that condition in the service known as heat prostration. For instance, the records show that in 1898, when owing to the Spanish-American War there were relatively large number of recruits and several summer months of general tropical cruising, though chiefly at reduced speed, the admission ratio for cruising ships was 29.4.

. . . . At present the nature of the so-called heat prostrations in fire rooms is not well understood. It appears that when men are working in hot air they are able to perform their duties without much distress, when the standing of the wet bulb thermometer is not much above 81°, but when that bulb approaches 86° to 88° the disinclination to work becomes very marked. However, the form of heat prostration may not be due to the direct condition of contained air as shown by thermometer readings, but may be precipitated by rapid variations of skin temperature incident to exposure to drafts under ventilators in natural ventilation or to currents incident to assisted or forced drafts when applied to a

fire room already containing men who have been subjected to very high temperature.

"At any rate, it has seemed that the tendency to heat prostration has become quite marked at times just after assisted draft has been started. It may be considered that if fire rooms were kept under assisted draft the cases of heat cramps would be greatly diminished, but that the use of assisted draft only occasionally to meet special conditions may be responsible for a number of such cases at some particular time."

The air of fire rooms has probably always been of sufficient chemical purity so far as adequate oxygen and minimal carbon dioxide are concerned, and there is no evidence that carbon monoxide from the furnaces or coal oxidation on the floors has accumulated to produce any such toxic symptoms as are commonly attributed to heat. That this distress tending to heat prostration is a matter of heat and humidity preventing automatic cooling of the body by evaporation of sweat and by convection to circulating air, as shown last year by Mr. Leonard Hill, of London, was surmised years ago is indicated by the following extracts from sanitary reports:

Surgeon Geo. H. Cooke, reporting on the U. S. S. *Mohican*, in 1885, said:

"It was while cruising along the Mexican coast during the rainy season [July and August] and in the warm water and hot murky weather of that region that numerous cases of prostration from heat occurred, as well among the men on deck as with those in the fire room."

Surgeon John C. Wise, on the U. S. S. *Jamestown*, in 1886, said:

"Two deaths occurred during the year: one, a case of insolation happened when the thermometer stood at 85°, showing the importance of care in this respect, especially when there is great atmospheric humidity, which so often prevails in the West Indies."

There are probably few medical officers who would now fail to affirm the belief of Chevers, Manson, Castellani, and other eminent authorities that of the predisposing causes of heat-stroke, alcohol habituation, or even occasional alcoholism, is one of the greatest factors. While I personally believe the navy would be almost infinitely better off if total abstinence could be enforced, and the medical department and messes of ships quite as well administered, if no spiritous, vinous, or malt liquors were permitted on board ship, still, given men who frequently indulge, that there is another side to the practical question is evidenced by the following opinions and practices of former naval surgeons: P. A. Surgeon G. P. Lumsden, reporting on the U. S. S. *Boston* en route from New York to Jamaica and Central America, October, 1888, says:

"The firemen complained 'of the heat of the fire room, which

had a temperature of 140° , and several cases of heat exhaustion occurred; the first on October 6th, the second day out from Sandy Hook. After this one ounce of whisky was given each fireman, who brought a card from the engineer at the end of his watch. This seemed to have a beneficial effect, as there were fewer complaints after this, and they appeared to work more cheerfully. At Port Royal fifteen gallons of Jamaica rum were purchased by order of the captain, upon the recommendation of the surgeon, which was served out in one-ounce doses as stated above, and it lasted until within a few days of New York."

Surgeon E. H. Green, on the U. S. S. *Marblehead*, reported in 1894:

"The temperature of this [berth] deck with the dynamo running was from 90° to 92° , rendering it almost impossible to obtain refreshing rest. The fire room has had a temperature as high as 140° [the author observed it 186° , July 13, 1906]. Usually it is 120° , the engine room being from 105° to 110° . There were several cases of heat exhaustion, though none of them of a serious nature. While cruising in the tropics it was found necessary to give stimulants at the end of each watch: one and one-half ounces of rum were given, and it had good effect, as it kept the men up to their work, looking forward to the dram at the end of the watch, and it restored the exhausted system materially."

Surgeon Howard E. Ames' report on the U. S. S. *Detroit*, for 1895, says:

"It is here I will make a few remarks upon the engineer's force, based upon observations made upon this vessel, and which, I think, apply to the whole service. The modern warship is a series of small compartments, demanded for strength and security. This compartment system is followed in the coal bunkers. When under steam in hot weather, these bunkers are not properly ventilated, and in addition to this the heat is too great. The deficiency of fresh air is not so serious a defect as the high temperature which surrounds the men while working. During the summer we were up the Yang-tse River, and during that trip the temperature of the coal bunkers ranged from 115° to 127° , while the outside temperature on deck was from 95° to 100° . If the engineer's force is expected to maintain its efficiency it is important that some scheme be devised to overcome this excessive temperature. It is absurd to expect nature to overcome a temperature of 28° under such conditions, and no human being can work efficiently in such a temperature without permanent injury to his physical and vital constitution. Take in addition to the heat, the *motionless*, impure air of the bunkers, filled with coal dust, constantly clogging the sweat glands of the men, and a moment's thought will picture their deplorable condition. During the trip it was only by giving each fireman and coal-passer two ounces of whisky at the end of

his four-hour watch that we were able to keep them at work and accomplish the trip. We had several cases of heat prostration, none of which was fatal. The men at the end of the watch were almost collapsed, *streaming with perspiration*, accompanied by *stertorous breathing*, *rapid pulse*, and trembling limbs. The eight hours' rest was not sufficient to restore them sufficiently to consider them efficient men.

"This exhaustion was not due to the work, but to the abnormal conditions surrounding the workers. This is shown by the weight of the coal handled on this trying trip. The general consumption during one day was 26 tons, the daily average for the trip being 18 tons. If we admit that this average was handled twice, it would give us but 36 tons handled in twenty-four hours by 30 coal-passers, or 1.2 tons per day per man, and this work was not continued beyond four hours. Such light physical exertion under normal conditions would scarcely be appreciated in its effect on the physical organization of a healthy laboring man. In this case we are forced to consider the degraded air and the heat as the cause. We can practically eliminate the degraded air of the bunkers by considering the amount of work done under similar conditions, but in a temperature below that of the body. We are forced to admit that it is principally due to excessive heat."

Extract from report on the U. S. S. *Bennington*, 1898, by P. A. Surgeon E. P. Stone:

"The men of of the engineer's force, all of whom swing in the wing passages and after berth deck, after four hours of severe and arduous toil in the frightful temperature of from 140° to 150°, would come off watch and endeavor unsuccessfully to get rest and sleep in the only comparatively less trying temperature of from 90° to 100°. Unable to sleep, worn out with fatigue, and annoyed by prickly heat, it would be jaded and discouraged men who would respond to the next call to go below on watch. Is it to be wondered at that the medical officer is called upon to furnish stimulants to keep these men up to their duty? Is it to be expected that men in such a condition can do efficient work? And may not a fire-room force in such a plight seriously cripple the fighting efficiency of a ship, as my predecessor has pointed out in his report? . . . It has been the custom on this ship to give, when under way, each watch in the fire and engine rooms some liquor, either during or at the end of the watch. On our way here from San Diego I conformed to the custom after the first few days, principally for its mental effect on the men, as they expected it, and furnishing the liquor served to keep them contented. I have not had enough practical experience yet to feel like making a positive statement, but so far as my experience goes it has inclined me to be opposed to the issue of spirits to men subjected to high temperatures. It produces a temporary stimulation, but leaves the men ultimately

in a state of lessened resistance. I believe a better stimulant, and a useful prophylactic, is the administration of strychnine. In those cases of heat prostration that give rise to muscular cramps, I believe, theoretically, that subcutaneous injections of normal salt solution ought to give relief."

Extract from report on the U. S. S. *Massachusetts*, 1899, by Surgeon S. H. Dickson:

"I had been led to expect, under the circumstances of war and during a close blockade and operations in the tropics of such duration in the summer months, that many cases of heat prostration among the 100 men of the engineer force would be encountered. With fires lit all the time, and steam all over the ship; bottled up, so to speak, every night, with temperatures in the fire rooms frequently and for hours at a time from 144° to 150°, in the engine room rarely below 120°, conditions were constantly favorable for their development; and yet but fourteen cases in all were admitted to the sick list, and these occurred after the removal of the strain and excitement of actual hostilities, and none of them of a serious character. Careful hygienic measures, such as frequent opportunities for bathing and washing, and the intelligent and constant use of the ventilating blowers, supplying an abundance of fresh air, undoubtedly led to this result. On only one occasion, and for a brief period during the voyage from Porto Rico to Cuba, was it considered necessary to issue a small spirit ration to the engineer division. It put heart into the men and was productive of nothing but good. It was given to each watch on coming off duty and after they had washed and cooled off."

Extract from report on the U. S. S. *Columbia*, 1899, by Surgeon C. G. Herndon:

"A number of men at various times were more or less overcome by heat in the dynamo, engine, and fire rooms, and were promptly brought to the sick quarters. The heart and not the brain was the organ which had given out among these men. The routine practice was to stretch the man out on the cofferdam, with the head low, loosen all tight clothing, and give him a liberal dose of whisky or brandy, with digitalis. Usually in a short time he would go off into a quiet sleep, and wake up ready for work.

"I am opposed to the routine issue of alcohol to the men below while on watch; but from my experience, and more particularly on this ship, I believe it would be well, if the Bureau sees fit to do so, to increase the amount of whisky in the medical supplies and allow the medical officers to give it to deserving men coming off watch when they show markedly the effects of the long exposure to the high temperature in which they work.

"I have seen various stimulants used, but nothing, in my experience and belief, does these men as much good when coming off

watch as a ration of whisky diluted with water, and, if necessary, with some digitalis added."

Surgeon M. H. Simons, on the U. S. S. *Iowa*, 1899, reported:

"During the trip to San Juan, and on one or two other occasions when the heat was great, the men in the engine and fire rooms drank so much warm water that nausea and vomiting often occurred, and nothing would be retained. We found that under these circumstances the trouble could be checked and even avoided by a moderate dose of alcoholic stimulant (part of the time we used alcohol itself), with capsicum, gentian, or hydrastis. This dose seemed to put the stomach in proper tone for the digestion of food, and to lessen the thirst. As a preventive it was given when the men came off watch. Heat prostration was treated by putting the man in a bunk with a wet towel over his face and head and giving 0.6 gram of acetanilid; in one hour, if the temperature still stood above 100°, 0.3 gram was given until the temperature stood below 100°, and then a bath was given, in which the patient lay for fifteen minutes; the water was at first warm and then gradually cooled to the temperature of the sea water in the pipes, probably about 76°. The acetanilid equalized the circulation and subdued the nervous symptoms; the lukewarm bath seemed to aid this and to exert a specially and noticeably good effect on the digestive tract."

In discussing "The Alcohol Question in the Navy," Medical Director P. A. Lovering, who was surgeon of the U. S. S. *Oregon* during the Spanish-American War, stated:

"I remember that on the cruise of the *Oregon* around from San Francisco, Captain Clark every day at his own expense furnished the firemen coming off the afternoon watch with a drink of spirits. It encouraged the men, did good, and I was glad that I could recommend it as a beneficial measure."

From our more recent knowledge of the precise nature of the action of alcohol in small doses it seems evident that the benefits noted in the foregoing reports were psychical and doubtless attributable to the narcotic effect; alcohol in these cases probably induced a more comfortable frame of mind, indicating consideration upon the part of officers in authority, and withal favored relaxation akin to that sometimes given after disease or injury to relieve undue apprehension. It is significant that no naval reports of the last decade refer to the use of alcohol either in prophylaxis or treatment.

With reference to the well-known advantage of having ships painted with light reflecting surface, Medical Inspector T. C. Walton, reporting on the U. S. S. *Chicago*, in 1899, says:

"Changing the color of the outside of the ship from black to white is believed to have lowered the temperature on this [gun] deck, during the summer days when the sun shone on the ship's sides, from 4° to 6°. . . . During the speed trials of this

ship at Newport in September last the temperature in those parts of the engine rooms was recorded as high as 129°. The air at the time was laden with moisture from escaping steam. A prolonged stay there was described as being unbearable. The engineers on duty were quickly prostrated. Efficient ventilation was urged."

Inadequate ventilation and removal of heated air on the earlier all-steam propelled ships is attested by the following quotations:

Medical Inspector G. W. Woods reported on the U. S. S. *Charleston* in 1890:

"The heat of the dynamo room is often so great that the thermometers, indexed for 140°, cannot register the temperature, and the men perform their work entirely naked, complaining of nausea and vertigo whenever the revolutions of the little electric blower are even for a brief period suspended."

Surgeon T. H. Streets reported on the U. S. S. *Bennington* in 1893:

"The temperature of the fire room previous to these changes [new hatch opened and new ventilators] was frequently as high as from 140° to 150°. The temperature has been materially reduced. The highest it has reached since the opening of the hatch is 112°."

On the U. S. S. *New York* January 11, 1894, Medical Inspector Edward Kershner found the temperature of living and working spaces to range from 88° to 108° throughout the ship when the outside air registered 82°, although the trade winds blew at the rate of 6 knots on the port bow, the ship making 13 knots under but four boilers, and burning but eighty-five tons of coal per day.

Likewise in 1894 Surgeon W. G. Farwell reported on the U. S. S. *Columbia*:

"The temperature of the engine and fire rooms is excessive when firing hard; the temperature of the fire room ranges from 140° to 150°, and that of the engine room from 105° to 110°; when firing immediately the temperature is respectively from 120° to 125° and from 98° to 100°. . . . the temperature of the cabins opposite (the engine room hatches) was 90°, an almost unbearable degree of heat for a sleeping room."

The recording of excessively high temperatures was the rule rather than the exception for a few years prior to and immediately following the Spanish-American War of 1898.

Surgeon C. A. Siegfried reported on the U. S. S. *Cincinnati* in 1894:

"In the dynamo rooms by means of electric (additional) blowers the temperatures have been reduced 20°, and they now rarely rise above 110°. . . . The ventilation of the engine room is very unsatisfactory, and temperatures are recorded from 90° to 170°. . . . I have myself recorded fire-room temperatures as high as 168°. In the engine room, lower platform, the

average is about 102° , on the upper platform it frequently reaches 135° ."

Surgeon E. Z. Derr, on the U. S. S. *Raleigh* in 1894 and 1895, reported:

"The inadequacy of fire-room ventilation made itself manifest on the first trial trip to Hampton Roads. Steaming half power the temperature of the starboard forward fire room in the boiler interspace, five feet above the floor, reached 180° . Three men were exhausted by the heat. On September 10, steaming under the same easy conditions, it reached the same, and two men were exhausted. On September 11, 190° was recorded. On the fire-room galleries, where the blowers were located, the thermometer registered 205° , rendering it impossible for the men to superintend them, and accordingly they were not used. The fire rooms were therefore dependent upon natural ventilation alone, and that supplied by the ventilation was wholly inadequate to keep down the temperature."

Medical Inspector J. G. Ayres, on the U. S. S. *Olympia* in 1895, reported temperatures of 180° and above in two of the fire rooms which had no blowers.

Surgeon C. A. Siegfried, again in 1895, on the U. S. S. *Texas*, said:

"It is to me doubtful if any possible system of ventilation in some of these spaces would correct the high temperature ranging from 125° in dynamo rooms and redoubt to 170° in hydraulic pump rooms. When the ship is under way the heat becomes excessive and during the short periods of time when making steam trials last September the number of cases of heat exhaustion treated in one day, aggregated twelve. The hydraulic rooms furnished most victims, hence the more thorough covering of the hot metals, pipes, etc., with non-conducting materials becomes imperative."

The improvement made on the U. S. S. *Cincinnati* in 1895 is shown by the report of Surgeon L. B. Baldwin, in which he showed average temperatures of fire room No. 1 to be 143° , 188° , 187° , 184° , 189° , 191° , and 109° , with a maximum of 204° between June 30 and May 12. After some changes in the management of the blowers the average temperature was reduced to 126° and 139° , with a maximum of 170° . The average for the year in this fire room was 145.8° .

The Surgeon General's report of 1897, covering the year 1896, stated:

"Of the 59 cases of heat-stroke, 40 were caused by heat in fire and engine rooms, 7 of the latter being returned from the *Raleigh*, 5 from the *Indiana*, 4 each from the *Amphitrite* and *Massachusetts*, 3 from the *Maine*, *Newark*, and *San Francisco*, and 2 each from

the *Cincinnati*, *Alert*, and *Marion*, the remainder (5) occurring scattered, 1 on each ship."

Surgeon Robert Whiting, on the U. S. S. *Monterey* in 1895, reported:

"The continued strain of resisting the high degree of heat early began to tell upon the men of the engineers' force. The closed fire room of the *Monterey* has no outlet overhead, the doors opening on one side into the overheated engine room and on the other into the berth deck. The forced draft ventilation not being in use, it was discovered that the fire room was fed by hot air from the engines on one side and on the other by air that had been devitalized by use on the berth deck. The medical officer upon one of his inspections found the temperature as high as 147°. There were a number of cases of exhaustion and vomiting, most of which were treated without entry upon the sick list.

"The drills at general quarters, which were more frequently performed than any others, required the use of steam in the pump rooms underneath the ward-room officers' quarters and under the berth deck. It will be observed by reference to the temperature charts that these pump rooms registered the highest degree of heat, 180°. It required hours to bring the atmosphere in the ward-room down to 90° after these drills were concluded. The dynamo room, contiguous to the forward turret and underneath which the forward pump room is located, the main compartment of the berth deck separated from it by a steel bulkhead, suffered in similar fashion."

Surgeon James E. Gardiner's report on the U. S. S. *Amphitrite* in 1896, stated:

"So far the most serious trouble developed has been the one of the high temperature generated on the modern iron and steel ship filled with engines and imperfect means of ventilation so far devised to relieve the evil. From the records of the medical journal the suffering from this cause while the ship was cruising during the months of July and August was great. Temperatures as high as 183°, in the fire room are recorded, with 167°, given as the minimum during the twenty-four hours of that day. In the engine room for the same day are recorded 155° as maximum and 148° as minimum; the berth deck, 102° maximum; a state room in ward room, 98°. There were numerous cases of heat prostration, cases of myalgia, cramps, and sudden diarrheas. A board appointed by the commanding officer, after carefully collecting the data, made its report, and the ship was ordered to the navy yard at Norfolk, where the changes were made. Since then the conditions have greatly improved. No test as severe though as that of last summer's cruising has been made since the change, but it is believed that no such temperatures will again be reached."

Extensive temperature observations made by Medical Inspector

J. G. Ayres in the dynamo room of the U. S. S. *Olympia* in 1896 gave the maximum as 121° and mean as 113° for August and 113° and 105° for October. In the same year the dynamo room of the U. S. S. *Columbia* was found to have a temperature range from 110° to 125° , and the steam-steering room exceeded 120° , with defective ventilation.

The means for adequately heating certain living spaces in ships often proved intolerable to other compartments as is shown by Surgeon W. S. Dixon's comment on his own state room on the U. S. S. *Brooklyn* in 1897:

"No less than seventy-five feet of steam pipe (heating) are very close to the berth—some of it within two inches and none of it more distant than forty inches. Five pipes pass through the room, and four are separated from it only by a thin metal bulk-head. Until the five pipes (forty-five feet) had been additionally covered with felt, one could not sleep in the bunk. With an outside temperature of 19° , that of this room was 90° , as determined by reliable thermometers, and the air duct was delivering cold air in the room at the time. In one of the double berth rooms of the junior officers two thinly covered steam pipes pass along the whole length of the upper berth, and in such close proximity that a man of ordinary proportions could scarcely crowd in between the mattress and pipes. It would be impossible for anyone to sleep there while steam was being used to heat the ship."

Surgeon W. R. Du Bose reported from the U. S. S. *Terror* in 1897:

"Practically the ship has done no cruising, and exactly what temperatures will be experienced remains to be seen. In the short trips made the engine-room temperature has been 118° , the fire room 116° to 142° , generally 122° ; the forward turret machinery space, 124° . In the superstructure during a heated term in July and August a temperature of 110° was several times noted. No case of heat exhaustion has occurred."

Surgeon P. A. Lovering, on the U. S. S. *Oregon* in 1897, reported:

"The berth deck is also very warm, as it is over the main boilers, and in it is placed the auxillary fire room. When the vessel is underway the temperature often rises to 100° and even higher, and rarely falls below 85° . The forward compartment of the citadel is fairly lighted by twelve deck lights, but has no direct air supply. It is much cooler than the central compartments, as it is forward of the boilers.

"Each engine room has, besides the usual hatch, a blower for artificial ventilation. The temperature ranges between 90° and 100° when under way.

"Each of the eight fire rooms has a large ventilator, and also a blower for forced draft, which is used for ventilation. When under way the temperature has reached 135° , but is usually 5° to 10° lower. This temperature was in cool weather when the outside

air was 60° or less, and it is probable that in warmer weather the fire rooms will be much hotter.

"There have been no cases of heat prostration."

The protests of some of our medical officers during this period were almost pathetic, as is seen in the following extract from the report on the U. S. S. *Bennington*, in 1898, by Surgeon John W. Baker:

"We should build our ventilators larger and higher and make them more numerous; provide our fire rooms, bunkers, and engine rooms with fans on a large scale, until we no longer are content that men should, in these days of modern science, toil and labor in a vitiated atmosphere at a temperature varying from 130° to 170°, until they are temporarily exhausted or permanently disabled, and that, too, long before the period assigned to men who live on deck in fresh air and wholesome sunshine, and who are never called upon to make the physical exertion, save in unusual emergencies, that these men must make every day, if we would maintain our speed at sea, speed and turning in evolutions—in fact, the efficiency that is not only desirable but absolutely essential for our success in warfare, and for which our ships are constructed."

Surgeon M. H. Simons, reporting on the U. S. S. *Iowa*, in 1899, stated:

"The ventilation of the distiller room is entirely inadequate, and the temperature is so high (145°) frequently that the man neglects his watch on the gauge to stand under the small cool-air inlet. The exit shafts for hot air in the dynamo room are so small that half the hot air collects in one or the other ammunition passage, increasing greatly the discomforts of those who must work there, especially in battle. The temperature of the dynamo room varies from 107° to 125°

"The state rooms for the officers in the citadel, at sea, in warm weather, have a temperature range of from 93° to 100°, artificial light has to be used all the time."

Surgeon John M. Steele, on the U. S. S. *Monadnock*, in 1899, reported:

"On entering the tropical zone, where the temperature of the air and water are nearly the same, and high, about 84°, the vessel heated up rapidly and remained so.

"The hottest part of the vessel in which men live is the superstructure and warrant officers' quarters. The warrant officers' quarters are next to the dynamo room, and separated by an iron bulkhead, and in the forward room the temperature averages about 95°. In the superstructure is situated the cabin and ward room, officers' quarters, also the galley, the officers' water closets, and the mens' head. These apartments are directly over the fire and engine rooms, and the heat here is high and continuous night and day, with an average of about 94°. There is a slight remission in the early morning hours. In addition to hatchets, deck lights,

and air ports the present means of ventilation should apply to the superstructure, and an active method of introducing fresh air, which could be accomplished by two additional blowers, to force air into the entire vessel. This addition would combine the plenum and exhaust, which I believe is necessary for the best effect for the health of the crew."

From a better ventilated gunboat, the *Annapolis*, in 1898, Assistant Surgeon S. B. Palmer reported:

"No excessively high temperatures have been noted in the engine and fire rooms, the two cases of heat exhaustion of mild grade which were treated were men unaccustomed to this work."

Asbestos sheathing helped to alleviate suffering in the living quarters abaft the engine room trunk of the U. S. S. *New York*, in October, 1899, where the temperature had formerly ranged from 98° to 110°. Medical Inspector C. U. Gravatt urgently advocated similar insulation in the dynamo room and evaporating room.

All evaporators are nowadays well covered with asbestos, conserving heat for their more economical operation and promoting comfort for their tending.

The surgeon of the "Flying Squadron," Medical Inspector Paul Fitzsimons, for 1898, stated:

"The fleet blockaded Santiago for five weeks, lying off the entrance about two miles in the open sea. Fortunately the trade winds were usually fresh, and no one suffered from the heat on the main and gun decks. The berth deck was like an oven. It was heated on the outside by the sun and inside by three smokestacks, the battle ports were closed and a moderate amount of air was driven by the blowers. The warrant officers' rooms were uninhabitable. The awnings could not be spread, and after a time the men were permitted to sleep in the open instead of sweltering below. They would lie on the forecastle wrapped in blankets, and no ease of sickness was caused by it. The crew also worked in the sun coaling ship frequently without injury."

Since the Spanish-American War conditions have steadily improved and the unfavorable reports have come chiefly from the older armored ships, notably the *Monadnock*, *Massachusetts* (in the fire rooms of which Surgeon J. C. Byrnes reported in 1900 an occasional temperature of 210°, reduced 30° by changing location of blowers), *Monterey*, *Chicago*, *Iowa*, *Brooklyn*, *Illinois*, *Wisconsin*, *Albany*, *Oregon*, *Alabama*, *Newark*, *Kentucky*, *Colorado*, *Ohio*, and *West Virginia*. Many reports at hand from these sixteen vessels, while interesting, merely reiterate the high temperatures of the living and working quarters.

On the U. S. S. *Texas*, Surgeon H. E. Ames reported steering engine room temperatures of 110° to 115° and humidity "so great that there is no evaporation from the body . . . those of the crew who are stationed there at sea are exhausted at the end

of two hours. "The firemens' wash rooms were "from 130° to 145°," and of course the air was saturated with moisture. Fire-room temperature under natural draft was 150°.

From the U. S. S. *Wisconsin*, in 1906, Medical Inspector H. G. Beyer reported as follows:

"Battleships and monitors will always be the most uncomfortable ships in a climate such as this (Cavite). With perfect sanitary conditions the constant high temperature and humidity from within and without are bound to cause a steady lowering of the average physical and mental strength and endurance of every human being on board. This generally acknowledged fact makes frequent change of station, especially for battleships, not only desirable but imperative.

"During the passage of this vessel from Hongkong to Cavite, between December 28 and 30, 1905, a series of heat prostrations occurred. Of the 14 cases, 10 were firemen, 2 water-tenders, and 2 coal-passers. The symptoms varied but slightly in the different cases, and were chiefly those of collapse, with dizziness, headache, and severe cramps in the legs, thighs, arms, forearms, back, and abdomen. In no case was there embarrassment of speech, although loss of voice was noted in one fireman, who stated that this was his second attack. Two of the cases did not show distinct symptoms of heat prostration until some little time after leaving the fire room, and one of the two was found unconscious.

"These patients were at first rubbed with towels soaked in hot water, with excellent results. Some in whom the cramps were painful and distressing were rubbed with chloroform liniment. Rest, of course, was enjoined upon them, and all were off the list and on duty two days after the arrival of the ship in port.

"The direct cause of the outbreak was the heat in the fire room, from what is known as assisted draft. In assisted draft the fire room is made as tight as possible, the air inlets and the furnace outlets being the only places in open communication with the fire room. But, unlike what happens during forced draft, when the blowers have their speed increased, and the incoming volume of air is very much greater than under ordinary draft, in assisted draft the incoming current remains the same, or may even be reduced.

"Several points in connection with the occurrence of this interesting series of heat prostrations seem to be unusual. The temperature in the fire room was not excessive, and alone could scarcely account for so widespread an effect; the relative humidity of the atmosphere was very high, and the temperature and moisture of the atmosphere suddenly increased the day the prostrations occurred. The afternoon we left Hongkong officers and men wore blue with comfort; the next morning white was ordered because of the sudden climatic change."

Of the smaller cruisers and gunboats complaints of high tem-

peratures and humidity were made in reports from the *Petrel* (160°), *Isla de Luzon* (172°), *Albany* (136°), and *Princeton* (115°).

On the newly commissioned U. S. S. *Maine*, in 1903, Surgeon N. H. Drake recorded 45 cases of heat prostration:

"Fifteen admissions to the sick list for this condition and about thirty others were treated for vertigo and cramps in the muscles of abdomen and limbs. Only one of those admitted remained on the sick list more than two days, he being under treatment for five days. Many of those not admitted were excused for the whole or a portion of their watch below. This unusual number of cases was attributed to a combination of circumstances, viz., new men unfit for service in their ratings; varying temperatures caused by draughts and blowers; improper clothing of the men in the fire room; the use of too much cold water while on watch; drinking water unfit for use on account of chlorides, and extremely hard work in a climate to which many of them were unaccustomed."

Assistant Surgeon A. G. Grunwell, who later evolved the interesting theory that heat cramps might be occasioned by absorption of toxins of tetanus bacilli from intestinal contents, in 1900 treated heat stroke successfully by venesection in the walled city of Tientsin during the Boxer uprising.

The following extracts from the annual report of the Surgeon General of the Navy of 1909 show how recently heat affections seemed to deserve special attention.

"Heat exhaustion is less prevalent than it was two or three years ago for the reason that the small cruisers with poorly ventilated fire rooms have either been withdrawn from tropical service or placed out of commission. The opinion that heavy, muscular work has been a contributory essential, and that heat, humidity, and rapid cooling of the body are not the only causes, received some support from an observation of Passed Assistant Surgeon G. H. Hathaway, on the U. S. S. *Cheyenne*, which now burns oil fuel. This officer shows that 'during the standardization runs at maximum speed the temperature in the fire room rose to 140°, which is about 10° higher than under previous similar conditions when burning coal. Nevertheless, in this higher temperature no case of heat prostration occurred, nor during the cruise has any member of the engineer's force succumbed to the heat. It is thought that the slight amount of physical exertion required to regulate the burners, as compared 'to passing coal, enables the fire room watch to withstand a greater elevation of temperature. While cruising the number of men on duty in the fire room is reduced to about one-half those required for coal fuel, which is of some sanitary advantage.' . . . Just what factors enter into the causation of the condition known as 'heat prostration' observed in those exposed to excessive heat, either solar or artificial, particularly fire room, is not definitely known today. There have been a great many cases in the navy during past years, and though

in 1908 a fewer number than usual were reported, and although effort has been made and is being made to improve the condition under which the engineer's force performs its duties, there seems no immediate prospect that the condition will cease to be an important type of disability."

Although not occurring on shipboard it would be amiss not to include in these extensive quotations the cases mentioned in an extract from the report of Surgeon G. A. Lung on duty with the First Regiment of Marines in the Pekin Relief Expedition of 1900:

"Two types of heat stroke were observed. The more common one was exhibited with extreme fatigue, mental depression, weak circulation, with perhaps partial loss of consciousness. The other appeared more suddenly, and was marked by hard, fast pulse, suffused face, bloodshot eyes, complete unconsciousness, and perhaps delirium, with muscular spasms of the entire body. These cases would appear while the column was moving or immediately on coming to a rest. If on the march they would stumble and fall in the roadway, or while sitting would suddenly topple over. The first intimation the medical officer would have would be the cry with stentorian insistence for the doctor, and on some days it came with startling frequency. They were carried to one side, an imperfect shelter from the sun for the head made by bending several standing cornstalks together and the best remedies at hand applied. If the patient appeared seriously ill a man was left with him, or several thus affected would be gathered together and one man look after all. In the meantime the column would move on, leaving them behind. The number who had convulsions was comparatively small. A large percentage became unconscious.

"August 10, was a peculiarly trying day, because of the heat. By noon fully seventy-five of the regiment had dropped out. It is true some of these were only badly wearied, and found an example in those who were more than wearied. There was, however, no shirking or malingering. Every man seemed to realize the character of the expedition and the purpose for which it was made. Indeed, it was sometimes touching to see a man with a determined expression trudging along, staggering from weakness and the weight of his accoutrements, and with a degree of illness that entitled him to a bed in a hospital. A few of the men, instead of dropping out at once, would gradually drop to the rear, where they would totter along, crying like a lost child, until relieved of their burden by a companion or forced to lie down and rest.

"A most remarkable feature of these cases of heat-stroke was the rapidity with which they recovered. Often without any treatment whatever, and by night, all by helping one another, or by getting a lift in a wagon or a ride on a horse, would overtake the column encamped for the night. The following day they would take their places in the ranks again. If the expedition happened

to be near the river and junks were available the worst cases were sent on them for a day's rest.

"There were but two deaths from this cause, one occurring at the battle of Yangsung, and the other at Tungchow. Two were afflicted with mild melancholia, but after a short rest in the hospital they recovered."

Undoubtedly the most complete report on heat cramps by medical officers of the navy in recent years are those of Surgeon M. S. Elliott in the *Military Surgeon*, for March, 1908, and of Surgeon A. G. Grunwell in the *United States Naval Medical Bulletin*, for July, 1909; their clinical notes are too extensive to be quoted here and from the one autopsy by Elliott the only characteristic pathologic condition found was congestion of the kidneys.

Sun-stroke as typically occurring in the midsummer heat of our cities is now comparatively rare in the navy, the last published case being one observed by me off Acajutla, Salvador, in 1907, in the person of a boat-keeper of the U. S. S. *Marblehead*, who fell asleep and became unconscious in his boat, without awning cover, and experienced total amnesia for sixty-nine hours. Thermic fever does not appear to have been an important factor since the Spanish-American War, when 89 cases were recorded. During the twenty-five years from 1886 to 1910 inclusive there were returned 1507 heat cases, of which 64 per cent. were heat prostration (commonly of the exhaustion type), 32 per cent. were classified as thermic fever, and 4 per cent. as insolation. About one-third of the cases of thermic fever developed on shore, and doubtless the larger part of the few on board ship were ill-defined confusion cases.

So far as I can learn heat-stroke between decks among men not performing hard work is unknown in our navy; if it were now common for persons to be stricken in cabins or while asleep we should certainly look for the condition among our ten thousand man-o'-war-men here about Key West and Cuba during the midsummer.

From the recorded and personally received opinions of naval medical officers I feel justified in affirming that the characteristic heat affection of the naval personnel has during the past quarter century been "prostratio thermica," heat exhaustion, largely confined to the fire room force; during 1909 and 1910 respectively, the admission rates per thousand for heat affection in the fire-room force were 8.45 and 7.91 respectively, while for the entire service they were 2.79 and 2.16 respectively, every other occupational group having ratios below the mean with the exception of the engineers' force, which were 3.26 and 2.78 for the respective years. This most common form, heat exhaustion, is believed to be a disease entity with either the systemic or muscular symptoms predominating, sometimes the one form almost to the exclusion of the other. The heat regulation centres do not appear to be so profoundly

incapacitated as in sun-stroke, there being but slight fever or very commonly the subnormal temperature of shock; Marine Oberasistenzarzt Dr. Esch, however, considered his case chiefly one of deranged nerve centres.

There is pallor or lividity, drenching perspiration, weakness of both voluntary and involuntary muscles, the circulatory and respiratory functions being profoundly embarrassed. Sensory motor phenomena are those of exhaustion rather than of the irritable, responsive to the least stimulation, type—there is the tendency to sleep and stupor rather than to convulsions. Now, although paradoxical, it is no inconsistency that the other notable symptoms may become prominent such as fibrillary twitchings and violent painful cramps of muscles of the abdomen, arms, and legs; these can hardly be due to any systemic nerve poison, but must be consequent upon a local dehydration of muscle tissue, with a diminished alkalinity of plasma from excessive production and retention of katabolic acids (sarcolactic, carbonic, and lactic), which have been shown by McDougall and E. B. Meigs to attend muscle rigor; the accumulation of products of tissue metabolism generally may account for vasomotor paresis and shock. It is, of course, important to distinguish cases of intestinal cramps due to dietetic error or ice water ingestion from the heat cramps of abdominal wall muscles.

The etiology and incipency of heat exhaustion need not be at variance with those of sun stroke except in intensity; the assumption is tenable that in sun stroke the factors are so fulminating and of such an overwhelming character that heat production and loss are promptly deranged, whereas the symptoms of heat exhaustion represent the sustaining and finally, failing efforts upon the part of the human body to overcome its adverse environment. I shall be content to enumerate these factors in causation of heat exhaustion, no one of which has been certainly eliminated as either contributory or immediate; no special combination seems to be essentially determining: Chronic alcoholism with fatty infiltration of the heart—dilatation when called upon to pump more blood through lungs and skin under stimulation of excessive heat; dissipation or debility from disease or unsuitable hygiene, such as overcrowding; hard muscular work (Edsall) and unrelieved fatigue; insufficient circulation of air and wet-bulb temperature from 85° to 95° (J. S. Haldane's critical point and Harvey Sutton's vicious circle); lack of habituation; constricting or heavy clothing; fright or panic induced by occurrence of other cases, as shown by Oswald Rees, R. N.; loss of sleep (H. M. Welch); improper nutritive ratio—excess of protein and deficiency of carbohydrates; insufficient assimilation of water; to these may be added Senftleben's observation of blood concentration, red-corpuscle destruction and hemoglobinemia more commonly expected in sun-stroke; arterial anemia, toxin and fibrin ferment accumulation from preponderance of skin over kidney excretion and leukocyte destruction (Maurice

de Fleury); predisposition by former attacks (W. H. Cameron and Logan Clendening); the actinic theory of Lieut. Col. R. J. S. Simpson is merely mentioned to be excluded in our cases among the fire-room force.

For the physiologist no doubt the inclusion of so many causative factors, direct or remote, is unsatisfactory, confusing, and a confession of ignorance; for the hygienist their probable relation has given such hints that the removal of few or many has contributed to the great decline in heat exhaustion and cramps in the navy. If I were called upon to single out any one remedy to bring about this result more than another it would be the increased circulation of air where the men work rather than any mere lowering of temperature or humidity.

STATISTICAL TABLE OF HEAT AFFECTIONS IN THE UNITED STATES NAVY AND MARINE CORPS, 1861-1911.

Year.	Mean strength (medical returns).	Cases.	To hospital.	Invalided from service.	Deaths.	Number of sick days.	Total damage in percentage of sick.
1861	20,000	5					
1862	25,905	34					
1863	40,000	16					
1864	43,787	27					
1865	32,641	3			1		
1866	17,193						
to	No data available in published reports						Apparently all insolation.
1872	11,570						
1873	12,723	14					
1874	13,870	19					
1875	10,141	5			1		
1876	11,138	8					
1877	7,461	17	"Heat exhaustion" (2 cases); first mentioned on Asiatic station.				
1878	7,806	10				26	.000791
1879	8,869	Not mentioned in reports.					.000000
1880	9,003	23		5		89	.026668
1881	9,546	18	3	1		50	.005729
1882	9,371	12	1			61	.001576
1883	9,197	10	1	1		166	.009670
1884	9,959	18				72	.001797
		"Heat exhaustion" really begins.					
1885	9,191	20	1			103	.003070
1886	9,188	5			1	20	.005442
1887	9,618	41	1			226	.006438
1888	9,955	25			1	96	.007657
1889	11,219	33	3			216	.005275
1890	11,768	37				257	.005983
1891	11,501	41	3			195	.004645
1892	11,775	29	2		1	135	.007760
1893	12,109	51	1	1		293	.010758
1894	12,520	44			2	190	.012145
1895	12,671	92			1	359	.011562
1896	13,768	59	3		1	257	.008622
1897	15,229	81	4		1	339	.010356
1898	23,038	512	19	7		2054	.039019
1899	20,113	154	10	1	1	939	.017594
1900	22,977	128	13		5	442	.015798
1901	26,101	95	4	2	1	643	.012352
1902	30,249	95	5	1	1	503	.007757
1903	36,534	94	2	1	2	333	.006543
1904	39,450	92	13			569	.003941
1905	39,620	160	3			655	.004529
1906	41,690	168	15	3	1	739	.009559
1907	44,083	86	4	4		504	.007448
1908	50,984	106	17	1		801	.005220
1909	55,550	155	6	3		703	.006090
1910	56,721	125		1		391	.002755
1911	61,399	88		1	1	423	.003516

REVIEWS

A PRACTICAL TREATISE ON FRACTURES AND DISLOCATIONS. By LEWIS A. STIMSON, B.A., M.D., LL.D. (Yale), Professor of Surgery in Cornell University Medical College, New York; Consulting Surgeon to the New York, Bellevue, St. John's and Christ Hospitals; Corresponding Member of the Société de Chirurgie of Paris. Seventh edition, revised and enlarged. Pp. 930; 498 illustrations. New York and Philadelphia: Lea & Febiger, 1912.

As a worthy successor to Malgaigne, Hamilton, and Gurlt, Stimson's monograph has long been the standard work on fractures and dislocations. It has now reached the dignity of a seventh edition. More than a hundred new illustrations have been added, and though in this way, as well as by numerous additions to the text, the number of pages has been increased by about eighty, yet the bulk of the volume has been skilfully reduced.

The book is too well known to require extended analysis, but a few references to matters of current discussion may be pardoned.

Dr. Stimson does not advocate operative reduction or direct fixation of fractures. He says: "The cases of fracture of the shaft of a long bone in which sufficient reduction cannot be maintained by a suitable external dressing are very rare. The cases are more frequent in which it cannot be completely made, or in which it cannot be certainly maintained during the application of the dressing. To make complete reduction exposure of the seat of fracture may be necessary, and in some fractures thus exposed and in some compound ones temporary direct fixation of the fragments may be advisable." He still maintains "that the presence of a foreign body, even if sterile and unconnected with suppuration in bone at or near the line of fracture notably exaggerates and prolongs the preliminary rarefaction of bone. I believe this influence may even cause failure of union" He believes silk and silkworm gut are less injurious than wire, and has no good words for Lane's steel plates. To Lane's claim that this absorption of bone does not take place if the fixation is solid, and the operation is done with minute attention to detail, Stimson replies, "That may be so. I do not know; but the evidence is overwhelming that, as currently applied, a wire or nail passing across the line of fracture does have this effect;" and he concludes that it is "unquestionable that the results of the general use of Mr. Lane's method would not materially differ from those

heretofore obtained by other fixation methods, and it is therefore by the results of those other methods, and not by Mr. Lane's, that the propriety of open fixation is to be judged."

In fractures of the neck of the femur he is satisfied with the reduction secured by that amount of abduction which is produced by longitudinal traction, with the slight tilting of the pelvis which is its consequence. Wide abduction, to secure forcible reduction, he condemns. He says: "No abduction which is wider than a normal neck will permit can create a normal neck. The alleged use of contact between the top of the great trochanter and the ilium as a fulcrum for such abduction is fanciful; no dissected hip that I have examined would permit the trochanter to be brought within an inch of such contact while the head remained in its socket." He adds: "Outward traction upon the upper part of the thigh, by weight and pulley, and a band passing about the inner side of the thigh, has been occasionally employed. I doubt both its efficiency and its advisability if efficient."

He adheres to the pathogenetical classification of fractures about the ankle-joint, the two main types being those by eversion and those by inversion. Of late objections have been made to this classification because not only are the patients frequently unable to describe how their injury was received, but also because it is claimed that similar accidents produce dissimilar lesions. Destot, Quénu, Clermont, and other recent students of the subject base their classifications on the lesions discovered by the x-rays, and disregard the pathogenesis. But though scientific accuracy may be on their side, Stimson's method undoubtedly has the merit of didactic simplicity. "The essential lesion," says Stimson, "is the tibiofibular diastasis." And of all the other proposed classifications we believe that proposed by Clermont, which has this lesion as its cornerstone, is the most accurate.

So much of interest is found in the portion of the work devoted to fractures, that it sometimes is forgotten that the section on dislocations is equally valuable and instructive. The most important additions in the present edition relate to the treatment of old dislocations; but of these we have left ourselves no room to write.

Throughout the work is painstaking, systematic, encyclopædic, and lucid—in a word, a model text-book. It is the best work of its kind in existence.

A. P. C. A.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol I, Nos. 5 and 6, October and December. Philadelphia and London: W. B. Saunders Co., 1912.

THE October and December numbers of *Murphy's Clinics* conclude the first volume of this remarkable publication, notices

of which have appeared from time to time in the pages of this JOURNAL. The entire six numbers make a volume of 931 pages, with 165 illustrations, almost all of which are "inserts."

The exact relationship which Dr. Murphy bears to this periodical magazine never has been clearly defined. It appeared from the publishers' original announcements that his part was wholly passive, if such a word be allowable in describing so active and energetic a person as Dr. Murphy. What we mean to imply is that it appeared as if the enterprising publishers had sent their stenographer to attend these clinics, much as any other interested listener might attend, but of course with the avowed purpose of making notes for publication; and that of course this was done with Dr. Murphy's consent. Here, however, it appeared that Dr. Murphy's activity ceased. Certainly the first few numbers did not belie this supposition. They contained some startling and unsupported statements, many of them evidently uttered in the heat of argumentative reasoning; and the proofs seemed to have been read by no one who had any familiarity with surgery as an art or with its vast literature. These defects, for as such we regarded them, were dwelt upon in our previous reviews; and we are happy to say that (whether as a consequence or not) the later numbers, especially those now before us, show that at any rate some measure of editorial supervision has been exercised, though not yet are we allowed to know who the editor is. The early numbers caused considerable surprise, first that so accomplished a surgeon as Dr. Murphy should be willing to have his name attached to them in their unedited state, and second that he should ever have consented to an arrangement which put him in the position of having his teachings brought forth in seemingly unauthorized form. It was this very lack of authority which made us unwilling to accept, and which still makes us unwilling to accept some of the statements as an expression of Dr. Murphy's sincere convictions.

One other defect we believe should be remedied. While the exact dates of injury, of admission to the hospital, etc., frequently are given, yet the date of the lecture or operation never is mentioned; so that the duration of the condition before operation can only be inferred.

Apart from these criticisms, nothing but praise can be uttered. The wealth of material is remarkable; Murphy's dialectic and his familiarity with all departments of surgery are wonderful; the illustrations are admirable; the results of treatment are incomparable; and the work as a whole presents a fascination to the student of surgery which has rarely or never been equalled. In addition to all these factors of merit, there has been added a most useful and complete index. May we have many more volumes!

A. P. C. A.

PATHOLOGY AND TREATMENT OF DISEASES OF WOMEN. By A. MARTIN, Professor und Direktor und PH. JUNG, Professor und Oberarzt der Universitäts Frauenklinik in Griefswald. Only authorized English translation, written and edited by HENRY SCHMITZ, M.D., Professor of Gynecology, Chicago College of Medicine and Surgery; Medical Department, Valparaiso University; Attending Surgeon, St. Mary's of Nazareth Hospital; Attending Gynecologist, Frances E. Willard National Temperance Hospital, Chicago. 187 illustrations, 25 of which are in colors. Fourth edition. New York: Rebman Company, 1912.

THAT this book has passed through its fourth edition is sufficient proof of the favorable impression it has made upon the profession. Starting as a compilation of lectures which Martin delivered in a vacation postgraduate course at the University of Berlin, this last edition embraces not only a summary of the author's rich experience, but also a *resume* of the more important work that has appeared on the subject. The bibliography includes two hundred and eighty complete references which are in themselves of considerable value, since they mark in many instances the epoch-making contributions to gynecological literature. On the whole, the translation is well done, but throughout the book are several examples of literal translation at the expense of good English. In these days of many books on the same subject, it is extremely rare to find any originality either in the method of presentation or in the subject matter contained; an exception to this general rule is not found in this book. We say this not in the spirit of unfavorable criticism, but rather as a statement of fact to better enable the reader of this review to appreciate what the book offers. In less than five hundred pages, the authors present a comprehensive review of the whole subject of gynecology, including not only pathology and treatment, as the title implies, but symptomatology and diagnosis as well. The pathology of the various lesions is fully described not only in its gross and microscopic characteristics, but also in its practical bearing on the clinical picture; the theories of mooted questions are stated briefly but clearly. The book is especially valuable in its exhaustive descriptions of symptomatology and diagnosis where no effort is spared in presenting a clinical picture which includes the manifestations of each lesion even in its rarer phases. Treatment likewise receives its due share of attention, and embraces not only the accepted operative procedures, but also the local and general measures which may be applicable to the individual lesion. We can highly recommend this book as a concise presentation of the entire subject of gynecology from its scientific as well as its practical viewpoints.

F. E. K.

MANUAL OF SURGERY, REGIONAL SURGERY. By ALEXIS THOMSON, F.R.C.S. (Edin.), Professor of Surgery, University of Edinburgh, and ALEXANDER MILES, F.R.C.S. (Edin.), Surgeon to Edinburgh Royal Infirmary. Fourth edition. Vol. II; pp. 891; 274 illustrations. Vol. III; pp. 547, 220 illustrations. Edinburgh, Glasgow, and London: Henry Frowde and Hodder and Stoughton, 1912.

THE second of the three volumes into which this work is divided is devoted to regional surgery, and includes that of special regions as of the ear, nose, throat, and female genitalia, but not of the eye. The pages are unusually small for a book of such ambitious purposes, and emphasize the chief characteristic of the work, condensation. Each chapter begins with a brief summary of the surgical anatomy of the part discussed. In these days of systems of surgery, monographs, and voluminous papers on surgical topics, the text-books covering the whole field of surgery, by one or a few authors, are becoming scarce. The authors have demonstrated that they can still be made very serviceable. By careful elimination, avoidance of repetition, and the subordination of the unimportant to the important, they have produced a condensed text-book that will be particularly valuable to students and busy practitioners. The quotations from recent writers are numerous although there are very few references to the exact sources of the information. The discussion of operative treatment is very brief, which is to be explained by the fact that the third volume is devoted to operative surgery. Still it would help the reader of the second volume if cross references were employed to indicate where in the third volume the operative treatment of a given condition is more fully discussed. The illustrations are in the main photographic, and serve the purpose satisfactorily. A few, however, are not very serviceable. For instance, on page 257, there is an illustration of a suicidal cut throat wound, the space for which could be better filled in by text. Angina Ludovici, in the opinion of the reviewer, could be described more accurately. It is nothing more than a severe submaxillary cellulitis which has invaded the floor of the mouth and the pharynx with a resulting edema of the larynx, and a general realization of this fact will save many lives. Pus is seldom detected, not because it forms early and is under great tension, but in some cases because there is none present, and these are the worst cases, and in others because it is small in quantity and buried deeply under thick edematous tissue. Constitutional symptoms are not always marked, they are sometimes practically absent, but this does not lessen the danger. Bronchoscopy for the removal of foreign bodies from the bronchi should receive more attention. On the other hand, the preference over thoracoplasty given to the injection of Beck's bismuth is justified

by the recent literature. The advice to always operate on strangulated hernia as early as possible and to employ taxis only when operation is refused or contraindicated, is also in order.

The third volume, devoted to operative surgery, like the first on general and the second on regional surgery, represents a careful and skillful condensation. It is brought well up to date and affords to the busy surgeon, as well as to the student, a concise but clear description of the formal operations of general surgery. The special fields of the ophthalmologist, laryngologist, and gynecologist, are not invaded. The illustrations with few exceptions answer the purpose for which they were intended. This, however, cannot be said of a few, for instance, of Fig. 12 on page 23, illustrating the ligation of the internal mammary artery. In order that such an anatomical illustration may be easily understood, it should show clearly the sternum and clavicle, particularly the former. The only guide in the illustration is the nipple which is too variable in position and too far away from the artery to serve the purpose satisfactorily. For the control of hemorrhage in amputation at the hip-joint, preference is given to the preliminary ligation of the femoral or external iliac artery. MacEwen's manual method of compressing the abdominal aorta, Momborg's abdominal tourniquet, and Spence's skewers are all, apparently, preferred to Wyeth's pins, which receive very brief mention. Wyeth's method of amputation, which permits the use of his pins and a tourniquet, are not spoken of. Most American surgeons would disagree with this position. With a few exceptions like these, there is little to be criticised and much to be commended in this volume which, with the other two volumes, represent a valuable *resume* of modern surgery. In both volumes the work has been well done and should continue to receive the encouragement it deserves. T. T. T.

THEORY AND PRACTICE OF THYROID THERAPY. By HERBERT EWAN WALLER, M.R.C.S., England, L.R.C.P., London, Honorary Anesthetist Birmingham Dental Hospital. Pp. 154. London: John Bale, Sons & Danielsson, Ltd.

THE first impression one obtains after reading Waller's book is that there are apparently few diseases which have not their origin influenced by thyroid secretion and their course benefited by thyroid medication. He presents numerous conflicting theories for the causation of various diseases, and cites cases of seemingly opposite character, benefited by the same course of treatment, without explaining satisfactorily the rationale of such procedures. The importance of the relationship of thyroid secretion to calcium

assimilation is well emphasized, and valuable suggestions for the treatment of malnutrition and kindred diseases in children are given. Several plausible theories are advanced in explanation of the action of iodine on the thyroid gland in goitre and Graves' disease, and the influence of arsenic on thyroid activity is given as the reason of the value of the drug in such diseases as lymphadenoma, various skin affections, etc. Diverse opinions as to the action of the salicylates on thyroid secretion are mentioned, and even carcinoma and tuberculosis are brought into the realm of possible beneficiaries of thyroid medication.

Through the maze of conflicting theories and facts concerning the thyroid gland, much valuable information may be gleaned, especially relative to the best mode of administering the drug. The author "ventures to think that an account of my wanderings into this little known land may prove interesting to all, and perhaps of assistance to some in enabling them to penetrate still farther." As such the book has served a useful purpose and should be deservedly popular.

T. C. K.

ZAHNÄRZTLICHE CHIRURGIE. By PROF. DR. MED. FRITZ WILLIGER, Direktor der chirurgischen Abteilung des Königlichen zahnärztlichen Universitäts-Instituts zu Berlin. Second edition; pp. 142; 114 illustrations and 9 plates. Leipzig: Dr. Werner Klinkhardt.

IN this work are considered most of the important surgical diseases of the teeth and mouth, with full details of operative and after-treatment. The title of the book, *Dental Surgery*, seems inadequate, in view of the fact that it deals with conditions beyond the scope of dental practice, while at the same time it does not go into the details of the ordinary operations performed by the dentist.

The author justly lays great stress upon the importance of the x-rays in diagnosis—the most valuable means at our disposal in bringing to light obscure lesions of the jaws. Dental cysts are divided into two classes—follicular and radicular. It seems to us that the latter variety would better come under the term "chronic abscess," since it always follows infection from the pulp canal. Dentists would do well to follow more often the advice of the writer to remove all teeth or roots having sinuses opening upon the skin, instead of persisting in useless attempts at conservation of the offending teeth. The author condemns the extraction of the second molar in any case of difficult eruption of the third molar. Most authorities hold that extraction of the former is quite justifiable under some conditions, for example, where easy removal of

the second molar would allow the third molar to come up and take its place. The chisel and mallet used by the author should have no place in operations on the teeth and jaws when we have at hand a far superior instrument in the electric surgical engine. For most of the operations described in the book, local anesthesia with novocain is recommended, though a timely word of caution is given against its employment in acute infective processes. The bad after-effects of injection under pressure of a local anesthetic in the region of the jaws, not so much of the drug itself, but of the spreading of the inflammatory process, are too frequently seen to make it safe as a routine measure. Several subjects which seem to us to come within the scope of the specialist in this region have been omitted from the book. For example, fractures of the jaws, cleft palate, and ankylosis of the temporomandibular joint, should have a place just as much as dislocation of the lower jaw.

The text is illustrated by many good photographs and diagrams, and the book should be valuable to both physician and dentist as giving a concise presentation of the subject. No one after reading it will deny that the diagnosis and treatment of lesions of this somewhat neglected region form a true specialty.

R. H. I.

TEXT-BOOK OF OPHTHALMOLOGY IN THE FORM OF CLINICAL LECTURES. By DR. PAUL ROEMER, Professor of Ophthalmology at Griefswald. Translated by DR. MATTHIAS LANCKTON FOSTER, Member of the American Ophthalmological Society; Member of the American Academy of Ophthalmology and Oto-Laryngology. Vol. I, Pp. 275; 186 Illustrations in the Text and Thirteen Colored Plates. New York: Rebman Company, 1912.

THIS, the first volume, deals with the conjunctiva, cornea, iris, and lens. The first chapter contains a short description of the anatomy of those structures and of the methods of clinical examinations of the same. Their diseases are considered in the following three chapters. The form in which the work is cast, being that of clinical lectures, permits of a certain familiarity and vividness not found in the ordinary didactic text-books. Etiology and pathology are based on the latest discoveries in this field. The cell inclusions discovered by von Provaezek and Habersaeder in trachoma in the epithelial cells of the conjunctiva are referred to, as also Heymann's demonstration that these peculiar cell formations are present during a blennorrhoea, the relation of which to trachoma has not been fully established. As regards the genesis of senile cataract, the views of Becker, Schoen, Moerner, Hess, etc., are quite fully given. The author's own theory is that the

subcapsular senile cataract is a metabolic disease of the lens, due to the influence of some poison upon the protoplasm.

Clear descriptions are given of the tuberculin test and Wassermann reaction. In regard to the value of the latter, Leber is quoted, who found that between 80 and 90 per cent. of the patients with secondary or tertiary syphilis who have positive syphilitic eye diseases and 90 per cent. of those with diseases of the eye due to hereditary syphilis react positively. At the same time, sole dependence should not be placed on the outcome of the reaction, but each patient should be submitted to a thorough clinical examination.

We cannot pass this book without a tribute to the excellent work of the translator, Dr. M. L. Foster. (The first ten lectures were translated by the late Dr. P. W. Shedd.) Dr. Foster refers in his preface to the difficulty of reproducing the power, vividness, and force of the original German. He is to be congratulated upon his success in accomplishing this difficult task.

We look forward with pleasure to the remaining volumes, and bespeak for the work a wide circulation among all who are interested in ophthalmology.

T. B. S.

THE CARE OF THE SKIN AND HAIR. By WM. ALLEN PUSEY, A.M., M.D., Professor of Dermatology in the University of Illinois. Pp. 182; 3 illustrations. New York and London: D. Appleton & Co., 1912.

THE attractive little volume of Dr. Pusey should prove of worth both to the physician and to all those individuals who are interested in the proper care of the skin and the hair; particularly in regard to the preservation of their health. Although the subject is quite well covered, the clearness of description and the simplified manner of narration makes even the histological details understandable to any reader. The little volume fills a niche of its own, and is a clear answer to the many questions asked in regard to the hygiene of the skin and the nails. The important questions of sleep, exercise, fresh air, sunlight, diet, clothing, and bathing are fully discussed in regard to their influence on health. The injurious and also the beneficial soaps are described in some detail. The much-abused face powder is thoroughly analyzed. The concluding portions of the book are devoted to the commoner skin conditions, and a few preparations are mentioned for their treatment.

F. C. K.

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MEDICINE

UNDER THE CHARGE OF

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Erythrocyte Inclusions following Splenectomy.—O. ROTH (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 23) reports a case of congenital hemolytic jaundice; the spleen was removed in 1900, relieving the symptoms greatly. The blood showed diminished resistance of the red blood cells (minimum resistance 0.58 to 0.60 per cent. sodium chloride). It is probable, since the patient had jaundice from childhood that the condition was congenital jaundice and not "splenic anemia," as diagnosed at the operation. The unusual feature of the case was the blood finding. The red blood cells varied between 5,600,000 to 6,400,000; the hemoglobin between 100 to 114 per cent., while under observation in 1912. The red blood cells showed anisocytosis with a preponderance of small forms, but with no poikilocytosis. There were a moderate number of red cells with polychromatophilic staining; basophilic granules were infrequent, as were normoblasts. Nuclear particles in the erythrocytes were very abundant. In the fresh, unstained specimen it was evident that a large proportion of the red cells presented 1 to 2 round, quite refractive inclusions, which seemed to move somewhat, though slightly, within the cell. Generally they were the size of a very small coccus, but at times the diameter amounted to about one-sixth of that of the red blood cell. When the blood was stained with Giemsa's stain, it was seen that these bodies were red, structureless, sharply outlined bodies; they possessed all the characteristics of the Howell-Jolly bodies. Usually only one, rarely two bodies were seen. With May-Grünwald's stain, the bodies were stained blue, with Unna's polychrome methylene blue, they were bluish-red. They were very numerous, in one instance cells

containing them numbering 20,000 per c.mm. Furthermore, about one-half of the red cells presented very fine dots, stained blue with Giemsa's stain; usually there was one dot, or, at most, three in a cell. Many of the cells showing Howell's body contained these dots. The dots described are not identical with Weidenreich's chromatin dots, which stain red with Giemsa's stain, and are usually double in the cell.

Transfusion Fever.—H. FREUND (*Deutsch. Arch. f. klin. Med.*, 1912, cvi, 556) has found that the febrile reaction which follows intravenous transfusion of blood is produced even when the animal (rabbit) is given his own defibrinated blood. The cause of the fever, he has shown in his previous work, must be sought in the corpuscular elements of the blood, and since the relationship of clotting (defibrination) to breaking up of platelets is well known, attention was directed particularly to the platelets as the cause of transfusion fever. Injection of fresh, unclotted blood caused no elevation of temperature. Similarly, blood to which sodium citrate had been added produced no febrile reaction in 24 experiments, but when the citrated blood was shaken with glass pearls—this manipulation injuring the platelets, as previous observers have shown—fever was noted in 7 of 11 experiments. The nature of the pyrogenous substances in the platelets is not clear. The fibrin ferment, Freund thinks, is excluded. Whether the proteolytic ferment, which is abundant in the platelets is concerned in the production of the fever must be investigated. Several days after the second injection of platelets—occasionally after the first—the animals became weak, emaciated rapidly, and died (in all 30 experiments). Autopsy showed fatty degeneration of the liver, and, to a less extent, of the heart and kidneys, and a few small hemorrhages in the pleura and epicardium. The clinical course corresponded to that of “ferment intoxication.”

The Prevention and Cure of Beriberi.—FRASER and STANTON (*Lancet*, 1912, lxxxiii, 1005) recount their recent investigations on beriberi. Rice is rendered harmful by the milling and polishing process to which it is subjected. In this way there is removed from the grain some substances of high physiological importance, the absence of which results in the production of polyneuritis in fowls and beriberi in man, when a diet is consumed of which polished rice is the staple. This substance may be in itself essential to nerve nutrition, or act by rendering other substances available. It appeared possible that if the active substances could be separated from the mixture of the rice mills' polishings, and given in a readily available form, an agent might be obtained which would be of value in the treatment of patients suffering from beriberi. The fat-free polishings were extracted in alcohol, in which the active substance is soluble. With this solution fowls suffering from the disease experimentally produced and continued by polished-rice feeding were cured, 5 out of 6. Eight fowls fed on polished rice plus the extract remained in good health. The experiments demonstrate the value of such an extract as a curative and prophylactic agent. Rapid curative effects in humans must not be anticipated, as extensively degenerated nerves require time for their

regeneration; but patients placed under favorable conditions and receiving daily, after food, a dose of this extract will have their prospects of recovery enhanced, and their period of invalidism lessened.

The Relation of Gastric Secretion to Rheumatoid Arthritis.—The failure of alkalis to improve the joint affections in rheumatoid arthritis, although markedly successful in acute rheumatism, was noted by earliest observers. It seemed to the authors, WOODWARD and WALLIS (*Lancet*, 1912, clxxxiii, 942), that the absence of hydrochloric acid in the gastric juice of one class—hydrochloric acid being well known as a germicide—might explain the demarcation between cases with an apparently similar degree of pyogenic infection. The gastric juice after an Ewald test-meal, a piece of dry toast, and one pint of tea, was examined in 10 typical cases of chronic rheumatoid arthritis. There was a diminution of the free and combined hydrochloric acid in every case. An excess of mineral chlorides pointed to a process of neutralization. The lowered ferment activity was striking. The analyses closely resembled those in gastric carcinoma, and in the absence of further proof of the latter, it is evident some definite gastric changes are present in the rheumatoid arthritis. Confirmation to a certain extent was obtained by the relief on treatment based on these results—an acid mixture by mouth.

Etiology of Dementia Paralytica.—At the present day, it is almost universally claimed that dementia paralytica is a manifestation of syphilis. In the judgment of ROBERTSON (*Lancet*, 1912, clxxxiii, 872), a satisfactory case has been made out for no more than the fact that previous infection by the *Treponema pallidum* strongly predisposes to the development of dementia paralytica and tabes dorsalis. Robertson has isolated a number of the diphtheroid group of bacilli, *B. paralyticans*, which he believes to be of etiological importance. With hemoglobin containing media, the *Bacillus paralyticans* can be constantly demonstrated in the genito-urinary tract and nasal mucosa of the paralytic. The nasal infection can be traced along the lymphatics, through the base of the skull to the intracranial lymphatic system. A culture can be obtained from the spinal fluid in considerable number of the cases. Intraspinal injection of living cultures in rabbits has produced lesions in the cord identical with those which occur in the brain of the paralytic. Several animals did not develop paresis until eighteen months or two years later. Out of 16 animals infected by the genito-urinary tract, 10 have developed paresis. Further, it has proved to be a contagious venereal disease. Three male rabbits developed well-marked ataxia and paresis of the hind limbs, after being placed with females whose genital tracts had been infected with the bacillus. Finally, by vaccine treatment, cases of early tabes have been much improved. By intraspinal injection of an antiscrum produced in sheep, striking results have been obtained.

Sporotrichosis in the United States.—RUEDIGER (*Journal of Infectious Diseases*, 1912, xi, 193) has collected 47 cases of infection of the human subject with the *Sporothrix* fungus in the United States, and to these adds 10 new cases. Only 24 of these 57 cases were confirmed

by a cultural or microscopic diagnosis. Five-sixths of the total cases have been observed in the Missouri Valley of Kansas, Missouri, Iowa, Nebraska, South Dakota, and North Dakota. Of 22 authentic cases in North Dakota, every one occurred along the Missouri River. Ruediger believes the organism lives as a saprophyte upon grains, grasses, or other vegetation, from which the infection is contracted, rather than each case being related to another preëxisting case. The disease is most common among farm laborers, and the cases are nearly always isolated. In only two instances did a second case develop in an individual who had associated with a person suffering from the disease. There is no evidence for the infection in man being contracted by horses. Histologically the nodules in the early stages are made up of embryonal tissue infiltrated with plasma cells, and polymorphonuclear leukocytes, and occasional giant cells. Necrosis occurs later, and secondary infection with staphylococcus. It is easy to locate the sporothrix from these nodules, and they can be found in sections of the tissue.

Complement Fixation Test for Gonorrhea.—O'NEILL (*Boston Med. and Surg. Jour.*, 1912, clxvii, 464) has analyzed the results of application of the complement-fixation test for gonorrhea at the Massachusetts General Hospital. One hundred and nineteen urethral cases were divided into three classes: (1) 60 cases, with definite clinical manifestations, such as organisms, prostatitis, vesiculitis, or stricture, yielded 50 with a positive test. In the remaining 10 the infection was very remote. (2) Of 30 clinically negative cases, 9 were positive, 5 of whom acknowledged a recent infection. (3) Eighteen of 27 borderline cases were positive. These cases showed a few leukocytes or shreds in the urine after prostatic massage. Twenty-four of 48 cases of lesions in the lower female genital tract were positive, and all of these showed either gonococci or a discharge. There were 25 cases of arthritis, 10 of whom had evident genito-urinary gonorrheal lesions. All but one reacted positively; 2 of 4 with history only were positive. Twelve of 20 cases of pelvic disease were positive, all with history or present infection. In summary, the following is interesting: Cases with gonorrheal history, clinically uncured, 109; 95 positive, 14 negative. Cases with doubtful cure, 27; 9 positive, 18 negative. Cases with doubtful diagnosis, 16; 5 positive, 11 negative. Negative to gonorrheal history, 17; 17 negative. Negative by examination, 52; 9 positive, 43 negative.

The Production of Leukocytes in the Treatment of Mental Diseases.—Recognizing that some forms of mental disorder are due to toxins, many of them microbic in origin, BROWN and ROSS (*Journal of Mental Science*, 1912, lviii, 389) believed it justifiable if empiric, to stimulate, if possible, the natural defences against toxemia. Brown and Ross employed nucleic acid as a drug which will produce a leukocytosis. Nine patients were treated, 5 with acute delirious insanity, 2 with melancholia, 1 with dementia præcox of the catatonic type, and 1 with general paralysis. A 5 per cent. solution of nucleic acid diluted with normal saline was injected subcutaneously every second, third, or fourth day in doses increasing from 15 up to 60 minims. The tem-

perature invariably rose 1 to 1.5 degrees in twenty-four hours, and the increase in leukocytes occurred on the second day after the injection. The average counts of 8200 to 8800 before injection were increased to 20,000 and 30,000 without any change in the relative percentage of the different cells. The shorter the interval between the injections, and the larger the doses, the greater was the reaction obtained. Treatment was continued for 12 to 15 doses over two to three weeks. One of the melancholia cases became quieter and rational. The physical improvement and the decrease in acute excitement in the 3 cases of delirious insanity was marked. No change could be detected in the mental condition of the 5 remaining cases. Brown and Ross believe the procedure rational in principle, of proved utility, and they advise its further use.

Determinations of the Nitrogen and Salt Content of the Sweat of Nephritics.—P. TACHAU (*Deutsch. Arch. f. klin. Med.*, 1912, cvii, 305) has determined quantitatively the nitrogen and sodium chloride of the sweat in a series of nephritides, the object being to determine to what extent the sweat bath relieves the diseased kidneys. The baths were continued in each instance for one hour, and all the sweat was collected. For nitrogen surprisingly low values were obtained. The highest excretion amounted to only 0.49 gram of nitrogen (1 case), usually only about one-half this amount or less. The chlorides, on the other hand, varied between 1.31 and 2.05 grams. Tachau, therefore, believes that any beneficial effects of sweat baths are not attributable to the removal of nitrogen through the skin. The withdrawal of sodium chloride, however, is sufficiently great to be of value, especially in edematous patients.

Clinical and Serological Studies of Paroxysmal Hemoglobinuria.—J. MATSUO (*Deutsch. Arch. f. klin. Med.*, 1912, cvii, 335) has had the opportunity of observing 11 cases of paroxysmal hemoglobinuria within the last year. A number of points of interest were brought out. In 10 of the cases cold alone precipitated the attacks; in the remaining case both cold and physical overexertion were capable of bringing on a paroxysm. In 4 of the patients there was acquired syphilis; in 7 lues was congenital. The hereditary nature of the condition was illustrated by its occurrence in a father and daughter, while in another case it was found that a sister and two cousins of the patient suffered from the disease. Serologically, all the patients exhibited autohemolysis after the original method of Donath and Landsteiner, though in some instances complement was exhausted, and it was necessary to add it before hemolysis occurred. Like other observers, Matsuo noticed that the autohemolysis was less pronounced the oftener the attacks of hemoglobinuria. Variation in the autohemolysis was dependent not only upon differences in the quantity of complement, but also of autohemolysin. In 45 per cent. of his cases, Matsuo has demonstrated isohemolysins in the blood. Usually, the red blood corpuscles of a hemoglobinuric whose blood contains isohemolysins are protected from the action of the isohemolysins of a second patient. Salvarsan was without effect on the course of the disease.

S U R G E R Y

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Intratracheal Insufflation Anesthesia.—COTTON and BOOTHBY (*Annals of Surgery*, 1912, lvii, 43) say that intratracheal insufflation or respiration is the only artificial method that absolutely provides for a sufficient aëration of the lungs, regardless of the respiratory movements of the patient, and that properly administered and safeguarded, it can be rendered devoid of intrinsic danger. In consequence, anesthesia by this method is indicated whenever the operation is about to interfere in any way with the ability of the patient to voluntarily respire. Therefore it ought to be used in all intrathoracic work, and in extensive operations about the head, neck, and mouth. Of the various anesthetics to be used with this method, ether with air, preferably supplied by a foot pump, is the most applicable for general use; however, nitrous oxide-oxygen with minimal quantities of ether may occasionally be the anesthetic of choice. To prevent deaths from emphysema, no matter what form of apparatus is used, it must be provided with a safety-valve by means of which the intrathoracic pressure cannot exceed 15 mm. of mercury.

Replacement of the Extirpated Bladder by the Cecum.—LENDEMANN (*Zentralbl. f. Chir.*, 1912, xxxix, 1697) calls attention to the very restricted employment of excision of carcinoma of the bladder and the very high mortality of the operations which have been done. He also calls attention to the operation performed by Makkas for exstrophy of the bladder, consisting in an anastomosis between the ileum and transverse colon, a division of the ascending colon with closure of the divided ends and the passage of the appendix through the abdominal wall to be used as a urethra. At a second operation the ureters with a piece of the bladder were implanted into the isolated cecum, which then became a substitute for the bladder and from which the urine escaped externally through the appendix opened at its external extremity. Lengemann says that little use has been made of the operation. He employed, without realizing it, a very similar operation, to permit the extirpation of a cancer of the bladder. The operation is summarized as follows: At the first sitting the cecum, ascending colon, and 30 cm. of the ileum were totally isolated. The proximal end of the ileum was implanted into the transverse colon near the sutured end. The

appendix was passed through the abdominal wall and the end removed. At the second sitting a few weeks later, after frequent irrigation of the "new bladder," the normal bladder was extirpated, the closed end of the ileum brought down, and the ureters implanted into this portion of the intestine. There was at first a marked constipation, followed by a severe diarrhœa. The urine was at first very cloudy with mucus and pus, notwithstanding the frequent irrigations. After some weeks the urine showed only some flakes of mucus. The new bladder contained 500 c.c., but the patient preferred the frequent introduction of a catheter, and was much pleased with the results. Among the advantages claimed for the operation were the following: Small danger of infection because of the absence of feces from the isolated piece of intestine. The ileocecal valve and peristalsis in the ileum offer a certain protection against backflow. The implantation of the ureters can be performed with much less tension into the movable end of the ileum than into the less movable cecum, as in Makkas' operation. The urine unmixed with feces does not cause dangerous absorption, and does not irritate the mucus membrane of the lower colon and rectum, as when the ureters are implanted into the sigmoid flexure. The new bladder contains easily 500 c.c. and is continent.

Stasis Hemorrhages Due to Traumatic Compression of the Trunk,—LANG (*Deutsch. Zeitschr. f. Chir.*, 1912, cxx, 76) presents an extensive study of this subject, and reports 7 cases, the first with much detail. In a traumatic compression of the trunk, from the increased intra-thoracic and intra-abdominal pressure, a backward pressure in the vessels is produced, most markedly in the large veins, which is transmitted in greatest part to the upper parts of the body and to a less extent to the lower parts. The chief effect is to be seen in stasis hemorrhages in various parts of the body. The increased blood pressure is due substantially to the passive compression of the body cavities, and therefore of the lumina of their contained vessels. If reflex "active factors" (closure of the glottis, body exertion) play a part, they only favor the extravasation of the blood from the vessels, but are not necessary factors. The almost constant skin ecchymoses in the region of the tributaries of the common facial vein, is due to valve insufficiency and impaired function of the intima duplicatures in these veins. The corresponding mucus membrane hemorrhages are due to similar causes. With a very high venous blood stream, in the presence of a decreasing blood pressure, the functionally competent valves may be insufficient against the impact. The relatively rare occurrence of intraocular hemorrhages and the complete absence of brain hemorrhages, is explained by a normal intraocular and intracerebral pressure, which, with the aid of the clothing (shirt collar, folds in the clothing) can prevent the occurrence of the extravasations. The brain veins are especially protected by a valve-like arrangement at the point of emergence of the sigmoid sinuses into the jugular veins.

The End Results of Double Fractures.—MOLINEUS (*Deutsch. Zeitschr. f. Chir.*, 1912, cxx, 137), under this title, discusses fracture from pronation of the foot, or the Dupuytren fracture. The clinical symptoms of this fracture are given as follows: (1) Marked swelling

of the region of the ankle, due to hemorrhage into the joint and surrounding tissues. (2) Displacement of the foot outward and at the same time backward, the axis of the leg passing out of the inner side of the foot. (3) Severe pain. (4) Abnormal mobility of the foot at the ankle-joint. (5) Indirect pressure pain from the calcaneus outward. It is absolutely necessary to give close attention to the reposition of the fractured ends of the bones, and much care to the fracture for a long time afterward. Good reposition is possible only by an overcorrection in supination, according to the severity of the case, and by preservation of this position by the dressing. This fracture should not be treated at home or by an ambulatory dressing, because without adequate assistance and sometimes deep narcosis, a proper dressing cannot be applied. The injury is of such a nature that it can be treated properly only in a hospital. At home the patient often leaves the bed too early and develops very serious secondary results. For a long time the callus is in a so-called rhachitic condition, that is, it is soft and yielding. Even if in the beginning or after supposed union with the foot in good position, too early use of the foot allows it to turn outward, so that the troublesome traumatic flat foot develops. After fourteen weeks it is usually necessary to correct the condition by operation.

Hypertrophic Arthritis.—JACOBSON (Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1912, xxv, 589) says that almost all authors handle chronic joint diseases differently. They have their own conceptions, classifications, and nomenclature. He concerns himself with the study of hypertrophic arthritis, and regards it as a well characterized disease. Its separation from other chronic joint diseases, especially those with atrophic degenerative processes, the progressive so-called chronic rheumatic affections, should not be difficult. Unlike them it is mono- or oligo-articular and is non-progressive. It affects males by preference. There are often palpable prominences and foreign bodies, and often joint creptitation. There is no ankylosis, and muscle atrophy is not very pronounced. There are rarely other trophic disturbances or marked constitutional disturbances. The x-rays show little bone atrophy, but always protuberances, and often cartilaginous or bony loose bodies in the joint without ankylosis formation. Often when the disease has existed only a short time, the x-rays show striking changes. The atrophic joint diseases often show only slight changes after they have existed a long time. The pathological anatomy shows that the hypertrophic alterations begin in the cartilage, the atrophic in the synovial membrane. The name "arthritis deformans" should not be employed. The adjective "hypertrophic," brings into prominence its most characteristic sign. In all other joint diseases the hypertrophic symptoms are absent and only to this disease can the name be applied with justice. In the treatment rest should be avoided and motion encouraged. While rest will relieve the pain, it leads to muscle atrophy, the avoidance of which is the most important indication. Even with the existence of a joint effusion, rest in bed or a fixation dressing should be employed as little as possible. In a remarkably short time muscle atrophy with all its unpleasant consequences, develop. These are impaired function, weakness, edema, etc., and

cause the patient to spare more and more the affected joint, and thus retard the improvement and healing for weeks and months. The movement therapy gives much better results. For those who cannot walk or stand, massage and medico-mechanical therapy is indicated. The hyperemia treatment is often indicated, either in the form of the hot air apparatus (active) or the suction apparatus (passive). Faradization can also aid. In some cases, usually those with hip-joint involvement, an orthopedic apparatus will be useful. Operation is restricted to cases with joint bodies, which impair very much the movements of the joints, cause much pain, or become caught. No noteworthy influence is exerted by the x-rays, as far as known, while radium should receive some consideration as a curative or at least an aid.

Round Ulcer of the Stomach and Duodenum as a "Secondary Disease."—ROSSLE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxx, 766) says that the round ulcer of the stomach and duodenum is a disease which is so frequently associated with certain other diseases and disturbances of health, that it must have some relationship with them. In many cases such a relationship can be shown that the round ulcer seems to be a "secondary disease." Its origin depends not upon transmission through the blood, but in all probability upon the reflex effect of nerve irritation. The experimental investigations up to the present time speak for irritation in the vagus region. These results in the stomach are of especial importance because of the dependence of the muscle movement and secretion upon the nerves. Erosions and ulcers are only different stages and grades of the same process. For the development of erosions, spasms of the muscularis mucosa may be of special importance, because the veins and arteries are occluded where they pass through the muscularis. This occlusion, according to the character of the concerned vessels, leads to hemorrhagic infarction or to ischemia, both of which are followed by local digestion necrosis of the mucus membrane, especially in the presence of hypersecretion. The places of predilection of the round ulcers are where the spasmodic folds of the musculature are especially prolonged.

Diagnosis and Treatment of Aneurysms of the Internal and External Carotids.—LIEBAULT and DAUDIN (*Arch. gén. d. Chir.*, 1912, vi, 1433) say that reports of cases of the internal carotid are not frequent and that those of the external carotid are still more rare. They had the opportunity of seeing one of each variety, with an interval between them of one month, and for this reason they undertook a study of the two conditions. In the case of the external carotid aneurysm, two catgut ligatures were placed around the external carotid artery above the superior thyroid branch and 1 cm. apart. The aneurysm gradually disappeared, and six months after the operation the good results were still maintained. The patient with the aneurysm of the internal carotid refused operation. If in a cervical tumor in the cervical or cervicopharyngeal, on inspection and palpation, pulsations synchronous with those of the pulse, are detected, and it is possible to register them with the sphygmograph, and if in addition the stethoscope permits one to hear a systolic bruit, the diagnosis of a carotid aneurysm is justified. If the aneurysm is located on the external carotid, it is often

only cervical. It is accompanied by pain, causes at times but not always a disappearance or a diminution of the intensity of the temporal pulse. Finally in its pharyngeal form it forces the tonsil directly inward, passing to a certain degree between the two pillars of the palatal arch. On the other hand the aneurysm of the internal carotid is never completely cervical. It is remarkably indolent and makes a prominence in the posterior and lateral wall of the pharynx, pushing the whole tonsillar region forward and inward, since it is posterior to the posterior pillar of the palatal arch. From the therapeutic standpoint the first of the 2 cases proves that in aneurysm of the external carotid, the constriction of the common carotid will, perhaps, be preferable to the ligature, diminishing the chances of rupture of the sac and favoring a cure, while respecting the cerebral circulation. This constriction can be obtained by a silk ligature or a metallic ring, or by plicating the arterial wall by suture.

THERAPEUTICS

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Neosalvarsan.—KERL (*Wien. klin. Woch.*, 1912, xxv, 1787) says that neosalvarsan is superior to salvarsan mainly because of its easy solubility in water. The remedy is at least equal to the older preparation in effectiveness. Many untoward by-effects have been observed following the use of neosalvarsan, but Kerl attributes these to the higher dosage given of neosalvarsan. He believes that untoward symptoms are less than with salvarsan, where equivalent amounts are given. Untoward by-effects are usually only observed after the first injection of neosalvarsan, therefore, it is advisable to begin the treatment, especially of cases in very active stages of syphilis, with smaller doses. It is also necessary, to avoid unpleasant symptoms, that the intervals between doses should not be too short.

Vaccine Therapy of Whooping Cough.—BAMBERGER (*Amer. Jour. of Diseases of Children*, 1913, v, 23) reports 6 cases treated with a vaccine prepared from several strains of the Bordet bacillus. The vaccine included the organism of the case treated, which he obtained by swabbing the throat and then flating the cultures until a pure culture was obtained. He gave 20,000,000 bacilli every other day, giving to individual cases from five to fifteen injections. There were no general symptoms, such as fever, rashes, malaise, general pain or vomiting, occurring as a result of the injections and only very slight local reactions at the site of the injections. The treatment did seem to lessen the severity of the disease, and shorten complications, although it did not seem to shorten the duration of the disease.

The Absorption of Digitoxin from Digitalis Preparations and its Relation to By-effects.—GOTTLIEB and OGAWA (*Münch. med. Woch.*, 1912, lix, 2265, 2339) find that digitoxin, the most active constituent of digitalis, is absorbed more rapidly from digipuratum than from digitalis infusion or the powdered leaves. The rapidity of absorption depends on a number of factors; stasis of the portal circulation may delay it considerably. They differentiate between two kinds of vomiting produced by digitalis: (1) That occurring within three hours after the administration of the drug, and caused by local irritation of the gastric mucous membrane; and (2) that beginning after six or seven hours, the result of the absorption of an excessive amount. They also found that digipuratum in solution is the most rapidly absorbed of all the digitalis preparations. Infusion of digitalis remains in the stomach a long time, and is the quickest to produce vomiting due to local irritation. The article fully confirms the clinical evidence that digipuratum is more quickly absorbed and less irritating to the stomach than are the infusion of digitalis and powdered leaves.

Duodenal Medication of Ipecac in the Treatment of Amebic Dysentery.—BECK (*Jour. Amer. Med. Assoc.*, 1912, lix, 2110) reviews the literature briefly as to the ipecac treatment of amebic dysentery. He is convinced that ipecac has a definite action on the amebæ, and, if properly administered, is undoubtedly the best remedy at our command. What is generally conceded, however, to be the proper method of administration proves such a formidable procedure that the treatment is wholly impracticable. In an attempt to overcome the many objectionable features of the methods in vogue, a simple, rational, and more practical method has suggested itself to him, in the use of the Einhorn duodenal tube. This tube was designed for duodenal aspiration and alimentation, and Beck thinks that it is an ideal instrument for the treatment of dysentery with ipecac. As a rule, patients have little difficulty in swallowing the tube, and comparatively little discomfort afterward. An examination of the stomach contents, to determine the presence of free hydrochloric acid, will help determine whether the tube has passed through the pylorus, which is done by aspirating a little of the fluid and testing with congo paper. After each aspiration the tube is washed out with a little water and clamped. When it has entered the duodenum, the aspiration is slower and more difficult, and the fluid is alkaline and bile-stained. The time required for the tube to pass into the duodenum varies from one to five or more hours. Beck says that ipecac is especially indicated in acute cases and in the exacerbations of the chronic forms. It is said by some clinicians to have practically no effect in cases in which the symptoms are due to a mixed infection. Beck reports 7 cases, all of the chronic type and refractory to other methods of treatment; 3 of these patients had complicating liver abscesses. Powdered ipecac was employed either suspended in mucilage of acacia or macerated in plain warm water. A 2-ounce metallic syringe was used to instil the remedy which represented from 1 to 2 drams of ipecac to the dose in a 6-ounce mixture. Unquestionably much of the success of the treatment depended on the quality of the drug. Those cases which required more than three or four doses, and in

which the amebæ reappeared in the stools were treated by a drug of an inferior quality. On the other hand, the cases treated with a physiologically tested powder yielded after the first or second dose. A detailed report of the cases treated is given, and Beek believes that his study of these few cases shows that the ipecac treatment by duodenal administration is distinctly more efficacious than by other methods. Many other forms of treatment had been employed without avail. The fact that this series of most intractable cases were either permanently cured or relieved for a considerable period of time bespeaks the efficiency of the method. Large duodenal doses of ipecac seem to have no injurious effects. There are occasionally gastro-intestinal symptoms such as nausea, less frequently, vomiting, and rarely diarrhea lasting from twenty to forty-eight hours. Slight general depression may appear with a tendency to lowering of blood-pressure, which rarely amounts to more than 10 mm., even with doses as large as 2 drams.

Effects of Subdural Injections of Leukocytes on Experimental Tuberculous Meningitis.—MANWARING (*Jour. Exper. Med.*, 1913, xvii, 1) found that rabbit leukocytes, injected into the basal meninges of dogs, in doses from 0.7 to 1 c.c., invariably cause death. Horse leukocytes, injected in the same amounts, cause death in about 25 per cent. of the dogs. The injection of foreign leukocytes into the meninges of monkeys causes few if any symptoms. The injection of from 1 to 3 c.c. of horse leukocytes into the meningeal cavities of dogs, simultaneously with the inoculation of the meninges with tubercle bacilli, causes a slight delay in the development of the paralytic symptoms in about half the treated animals. This delay, however, is very slight when compared with the remarkable prolongation of the latent period previously observed after treatment with dog leukocytes. The injection of foreign leukocytes into the meningeal cavities of monkeys has thus far given almost uniformly negative results. In one small group of monkeys, however, inoculated by the method of lumbar puncture, the injection of rabbit leukocytes has been associated with a prolongation of the latent period in one of the treated monkeys, and with a complete prevention of the subsequent tuberculosis in a second monkey.

The Relapses after the Use of Salvarsan.—GAUCHER (*Jour. des Praticiens*, 1912, xxvi, 737) believes that there is no doubt that grave consequences may follow the administration of salvarsan, such as blindness, deafness, various paralyses, arsenical polyneuritis, and death after even small doses. Gaucher is very pessimistic as to the value of salvarsan in the treatment of syphilis, and says that the plan of treatment now recommended by combining mercury with the salvarsan is a confession of the failure of the remedy. Gaucher admits that salvarsan may have a restricted use in syphilis. It is valuable in that it heals up superficial lesions, and prevents the spread of the contagion. Salvarsan may be used for patients who cannot tolerate mercury, or in cases where mercury fails to benefit, but he deprecates its general use for the treatment of syphilis. He discusses relapses following salvarsan treatment which he declares are almost invariably the

result if salvarsan is used alone. He reports 31 cases in detail where there was a relapse of syphilitic manifestations. These cases were taken at random from the records of his clinic at the St. Louis Hospital, and he mentions a number of other writers who have reported similar observations.

Action of Large Doses of Alkalies in Diabetes.—HANSEN (*Zeitschr. f. klin. Med.*, 1912, lxxvi, 219) gives the details of 8 cases of diabetic coma treated with sodium bicarbonate. He found that the effect of treatment was merely to postpone the coma, and that coma invariably recurred. All of these patients eventually died and, he gives the necropsy findings in his article. The weight was carefully observed in 15 cases of impending diabetic coma, and it was found to increase in every case from 0.1 to 12.4 kilos (27 pounds). This increase of weight is explained by a retention of water due to the alkali.

Salvarsan in the Treatment of Syphilitic and Metasyphilitic Diseases of the Nervous System.—DONATH (*Münch. med. Woch.*, 1912, lix, 2274, 2342) reports excellent results with the use of salvarsan in various diseases of the nervous system. The cases reported comprise 48 cases of syphilis of the central nervous system, divided into cerebral, cerebrospinal, and spinal syphilis. Donath also treated 31 cases of tabes and 28 cases of dementia paralytica with salvarsan alone, and also combined with mercury. The best results obtained were in the early stages of these two latter diseases. Donath's article includes details of some typical cases treated.

The Treatment of Diabetes Mellitus.—KRETSCHMER (*Berlin. klin. Woch.*, 1912, xlix, 2221) writes concerning hediosit, first recommended by Rosenfeld, which has the chemical formula $C_7H_{12}O_7$. This is recommended as a substitute for sugar in the dietary of diabetics. It has a sweet, pleasant taste, making it agreeable to take, and is much superior to other substitutes for sugar in that it can be oxidized and be of food value. The glycosuria is not only not increased by the administration of hediosit, but even seems to be diminished by its use. Kretschmer also states that it seems to increase the tolerance of the diabetic for other carbohydrates. With the exception of slight diarrhea when used in large amounts no untoward effects are observed from its administration. Kretschmer believes that it is a distinct addition to the dietary of diabetics and when given in doses of from 10 to 30 grams a day is easily oxidized and utilized in the chemistry of diabetics. He also recommends pantopon in doses of from 0.01 to 0.02 gram three times a day for the treatment of the severer types of diabetes. By its use he was able to cause a decrease in the amount of urine, and to a less extent also in the total quantity of sugar. This effect, however, is only temporary. The article is not very convincing as to the worth of hediosit.

Organic Iodine Preparations: their Pharmacology and Therapeutic Value.—MCLEAN (*Arch. of Int. Med.*, 1912, x, 505) draws the following conclusions with regard to the therapeutic uses of the organic

iodine compounds from evidence presented as to chemical nature, absorption, and excretion, distribution, physiologic action, and clinical results. Up to the present it has not been shown that the organic iodine preparations with the exception of preparations of thyroid, have any specific action in pathologic conditions, except the action of iodine after separation from the molecule. The iodized proteins seem to be of advantage for therapeutic use only insofar as they avoid gastric irritation. The more stable compounds are apparently not entirely split in the body, and are therefore not well utilized, while the less stable compounds have no advantages over the alkaline iodides, either as to local effects or as to rapidity of absorption and excretion. The iodized fats and fatty acids appear to have some advantage when the continuous action of small amounts of iodine is desired. They are more slowly and evenly split, and the amount of available iodine in the blood does not vary from time to time to the extent that it does when the alkaline iodides are administered. The use of the iodized fat in such conditions as arteriosclerosis, bronchial asthma, lead-poisoning, etc., probably has some rational basis, therefore, on physiologic grounds. These substances are also, as a rule, non-irritant to the stomach. The difference in frequency of iodism is probably due to the difference in the amount of available iodine present in the body at any one time. When large amounts of iodine are desired, as in cerebrospinal syphilis, avoiding the danger of iodism would be at the sacrifice of therapeutic efficiency. The use of organic iodide preparations with toxic side actions, due to the molecule or its splitting products, should, of course, be discouraged. The products of iodine with the higher fats and fatty acids are generally free from toxic actions.

PEDIATRICS

UNDER THE CHARGE OF

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The Histological Blood Picture in Infantile Scurvy: Occurrence in the School Age.—F. GLASER (*Berlin. klin. Woch.*, 1913, 1, 200) offers several typical cases in a study of the blood picture in infantile scurvy, and reports a case in a boy, aged seven years. Marked pallor commonly occurs in scurvy, but it is not generally known that histological blood pictures arise during the course of scurvy. The reaction of the bone marrow in infantile scurvy is slight, and the appearance of nucleated red cells is not connected with an aplastic condition of the marrow, but marks a definite blood picture in severe cases of scurvy, and is accompanied by abnormal form elements besides normoblasts and megaloblasts. One case reported here was in a child, aged seven months, who had been fed on boiled milk for a long period. The general symptoms were hemorrhages from the

mucous membranes, pain on moving the extremities, hematuria, changes in the cartilages of the long bones of the extremities, swelling along the tibiae, all of which showed marked improvement under antiscorbutic treatment. The blood picture showed hemoglobin, 40 per cent.; erythrocytes, 800,000; leukocytes, 12,000; polymorphonuclear cells, 40 per cent.; lymphocytes, 60 per cent.; eosinophiles, 1 per cent. There was slight poikilocytosis and polychromatophilia. Large numbers of megaloblasts, normoblasts, and transitional forms were found. Syphilis, tuberculosis, and pseudoleukemia were carefully excluded. In four weeks, under antiscorbutic treatment the blood picture was almost normal, the cartilage changes almost gone and the child fairly recovered. The case of scurvy in the boy, aged seven years, showed pallor, weakness, swollen, bleeding gums, pain on moving the limbs with tenderness on pressure, hematuria, and typical shadows at the cartilages of the long bones shown by x-ray plates. The child had been raised on boiled milk and bread, refusing all vegetables, meat, etc. Under raw milk and antiscorbutic treatment the condition cleared up in six weeks. The cartilage changes had also cleared up and showed no shadows under x-ray examination. Glaser, therefore, claims this a case of typical infantile scurvy in the school age, of which but 6 cases have been reported in literature.

The Pathogenesis and Etiology of Rachitis.—MAX KASSOWITZ (*Deutsch. med. Woch.*, 1913, xxxix, 201), in discussing an article by Ribbert on rachitis, agrees that the origin of the calcium deficiency in rachitic bones is not in calcium metabolism but in pathological changes in the bone-forming tissues and that these changes are set up by irritating substances in the circulation and soft tissues. He disagrees with Ribbert's views that the irritating substances arise from digestive disturbances due to improper milk feeding. Kassowitz's explanation of these substances rest on the following points: All pediatricists agree that well-developed cases of rachitis and marked softening of the bones of the skull, occur in normally nourished, breast-fed children: Again, in the summer time when gastro-intestinal irritations are most numerous and frequent, the curve of rachitis, both as to frequency and severity, sinks to a low point, while during the winter months when there is little gastro-intestinal trouble, the curve rises higher with each month. The nervous disturbances accompanying rickets follow the same rule. In tropical countries rickets is either unknown, or occurs in a few mild cases. These facts not only contradict Ribbert's view, but offer an explanation of the real origin of these substances. In our climate during the months in which rickets is most frequent, children and infants are housed in for weeks at a time. Rickets is primarily a disease of cities and especially frequent among that class who are poorly and unsanitarily housed. The frequency and severity of rickets increase with the number of persons living in the same room. Hansemann shows that children born in the fall and dying in the spring of the year show a large percentage of rickets, while those born in the spring and dying in the fall show few signs of rickets. Tests on the young of animals bear out this fact, notwithstanding the perfect feeding of the captive animals. In support also of the claim of Kassowitz, that the irritating sub-

stances are "respiratory poisons," is the fact that one finds a large number of infants born with a rachitic rosary and softened bones of the skull, and that these changes are found much more frequently in children born during the winter and spring than in the summer and fall, and are found much more frequently in infants whose mothers passed the months of their pregnancy in a large city, than in those whose mothers came to the city from the country at the time of confinement. These facts impress the truth that the impurities of the inspired air, especially present in the circumstances above mentioned, pass through the circulation direct to the bones and cause the rachitic changes there, where there is normally at that age a hyperemia. The same impurities in the poorly ventilated air space, entering the pregnant woman's circulation, are carried to the centres of ossification in the fetus and cause the groundwork of the rickets subsequently developing in the child.

The Normal Body Temperature of Children and the Effect of Exercise and Rest.—DORA FRAENKEL (*Deutsch. med. Woch.*, 1913, xxxix, 267) offers the results of an investigation on 163 children to determine the normal temperature per rectum and to find a cause for elevation of temperature so often found in normal, healthy children. Diurnal variations in temperature are frequently found in apparently healthy children, and some authors claim a daily elevation to 37.5° C. or 38° C. to be a significant indication of latent tuberculosis. Elevation in temperature in apparently healthy children has been explained by various authors as being due to adenoiditis, local overheating of the rectum from bacterial action, and nervous excitability in sensitive children. Almost all the children in the Borgsdorf institution showed an after-dinner (noon) temperature of from 37.6° C. to 38.5° C., without any physical symptom of illness to explain it. The children under observation numbered 137, aged between five and one-half and thirteen years, and 26, between fourteen and sixteen years. These children were free from adenoids and enlarged tonsils. Only those children were chosen who showed a morning and evening temperature, taken in bed, of 37.2° C., and over a period of three days. During the experiment the temperature of these children was taken by rectum, while still in bed at 7 A.M. It was again taken at 4.30 P.M. after an hour and a half unrestrained play and romping. It was taken a third time at 8 P.M., one hour after they had been put to bed. The thermometer was inserted $4\frac{1}{2}$ centimeters into the rectum and held there until the mercury stopped rising. All of the 163 children so tested showed an elevation of temperature in the afternoon, 4.30 o'clock. In 42 children the temperature rose to 37.6° C., in 85 children to 38° C., and in 36 children to above 38° C. In the first group, 39 children had a morning and evening temperature of 37.2° C.; 83 of the second group, 37.2° C.; and 35 of the third group, 37.2° C. To determine if the afternoon rise in temperature was due to the physical exertion of the play and romping, every child was put to bed immediately after the 4.30 P.M. record was taken. After one-half to one hour's rest in bed every child showed a temperature of 37.2° C., or below, and the longer the rest the lower the temperature was recorded. The tests were made daily for three weeks, and the

children again examined to determine their perfect health. The results of all the measurements were the same. Of the 163 children 113 showed a positive reaction with tuberculin (Pirquet's reaction), but the positive children differed in no respect from the negative ones, in the temperature reaction from bodily exercise. Fraenkel finds the normal temperature per rectum to be 37.2° C. in 96.3 per cent. of the children. The difference between rectum and axilla was never more than 0.5° C. Bodily exercise in all children increases the temperature to 38° C. and above, which drops to normal again after rest. Neuro-pathic children show a higher rise of temperature following exercise than normal children, when the atmospheric temperature is 16° to 25° C. or over.

Non-gonorrheal Conjunctivitis in the Newborn and Infants.—C. CREDE HORDER (*Deutsch. med. Woch.*, 1913, xxxix, 74) points out that frequently newborn infants and older babies suffer from a conjunctivitis which is not gonorrheal and which under proper treatment leaves no serious consequences. The habit of attributing all inflammations of the conjunctiva in the newborn to gonorrhea tends to invalidate statistics. Diagnosis of such conditions should always rest on microscopic examination, which would show gonorrheal inflammation to be less prevalent than is supposed. The non-gonorrheal conjunctivitis differ from the gonorrheal type in that the cornea is not involved and that the secretions are more serous than purulent and are less in amount. The microorganisms found in the non-gonorrheal type were studied by cultural methods and found to be most frequently a Gram-positive diplococcus, the pneumococcus, and the colon bacillus. Infection with the first-mentioned coccus occurs from the sixth to the sixteenth day of life, is mild in type, and has a serous secretion. Infections with the pneumococcus causes a much more severe inflammation with secretion of pus, edema, fibrinous exudate, and slight hemorrhages. The cornea remains intact and the course is from two to three weeks. Infection with the colon bacillus is milder, the secretions mostly serous, and the course from four to eight days. The treatment consists in frequent cleansing with solutions of boric acid and the instillation of weak solutions of the silver salts.

OBSTETRICS

UNDER THE CHARGE OF

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Intracranial Bleeding in the Newborn following Rupture of the Tentorium.—BENTHIN (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Bd. xxxvi, Heft 3) draws attention to the occurrence of this accident in newborn children, and believes it may be favored by improper methods of

protecting the perineum, if too great pressure be made against the perineum at the time of labor. In 1239 labors there occurred 8 deaths from rupture of the tentorium, probably caused by violent or sudden manipulation and unnatural pressure upon the head in efforts to prevent laceration of the perineum.

The Outdoor Treatment of Puerperal Infection.—YOUNG and WILLIAMS (*Boston Med. and Surg. Jour.*, 1912, No. 11) report the results of their investigations in the Boston City Hospital in the outdoor treatment of puerperal septic infection. The patient is kept out of doors in a wheeled bed, which can be moved into the ward when necessary. Sunlight seems to be as important as air, and except in hot weather the patient is placed directly in the sun. Iron and arsenic are valuable aids in restoring hemoglobin, and strychnine is a useful stimulant to the vascular and nervous system. Alcohol increases the appetite, preventing loss of flesh in prolonged cases. Fluids are given copiously by the mouth, and in severe cases salt solution by the bowel. If there is fever, alcohol and cold sponge baths are used. Abdominal distention is treated by hot or cold applications. Young and Williams believe that the outdoor treatment has reduced mortality in severe septic infection nearly 20 per cent. The treatment does good by increasing the amount of hemoglobin, and for this purpose sunlight is as important as fresh air. The use of the curette is contraindicated, as it increases mortality nearly 10 per cent. A single intrauterine douche of sterile salt solution may be used if indicated. The value of this is denied by some. Not much result has followed the use of antistreptococcic serum. The outdoor method is the most effective known at present for puerperal infections, for the reasons stated.

Pituitrin Extract in Inertia Uteri.—HUMPSTONE (*Amer. Jour. Obstet.*, September, 1912) reports his experience with pituitrin extract in the treatment of uterine inertia. He used pituitrin in 64 selected cases without unfavorable results to mother or child. The remedy is expensive, but in some cases is efficient. Two preparations were employed, one the vaporoles of pituitrin extract, made by Burroughs, Wellcome & Co., 1 cm. representing two decigrams of the fresh posterior lobe of the pituitary body; and pituitrin manufactured by Parke, Davis & Co., in ampules containing 1 c.c., representing 1 decigram of the fresh pituitary gland. Apparently the better results were obtained in the first described material. The remedy must be given hypodermically and in the substance of the muscles. The first dose varies from 1 decigram to 1 gram; 4 decigrams, or 4 c.c. of pituitrin solution was the first dose, repeated every twenty minutes, in three doses. No more was given if no result was obtained. The objection has been made that pituitrin raises blood pressure. With patients in labor this effect is not so pronounced as at first supposed. The highest elevation observed was 20 points, the average, 8. The lower the blood pressure in the beginning the greater was the elevation from the use of the drug. The pressure was continued for two hours. If blood pressure is over 150 at first, with a possible lesion of the heart or kidneys, the remedy should not be used; but if such is not the case,

its effect on blood pressure need not be feared. In early pregnancy the drug does not act as an abortifacient. Uterine contraction may result, but the contents will not be expelled. In the induction of labor, after the bag has been introduced, the remedy has some effect. It will not, however, bring on labor. The remedy should not be used before the cervix is shortened and dilated sufficiently to at least admit three fingers. When, however, labor has well started, and especially, after the membranes have ruptured, should delay from simple inertia occur, the remedy has proved efficient. In the second stage good results were seen by giving pituitrin and strychnine, gr. $\frac{1}{20}$, at the same time, hypodermically. [In these cases why was not the good effect obtained as the result of the administration of strychnine, which is a powerful and reliable tonic in labor? E. P. D.] In the third stage of labor with inertia and bleeding, pituitrin causes intermittent contractions of the uterus, and is thus inferior to ergot, which produces tonic contraction. Where immediate contraction is demanded, pituitrin is valuable. It seems also to favor involution. In 7 cases of Cesarean section, ergotole, 30 minims hypodermically, was given at the beginning of the operation. Pituitrin was administered after the sutures were placed in the uterus. In 6 of the 7 cases the results were favorable. In 1 case where pituitrin was given earlier in the operation the uterus contracted so promptly as to interfere with the placing of the sutures, and later on considerable hemorrhage occurred into the abdomen beneath the uterine peritoncum, forming a hematoma which was afterward absorbed.

Primary Uterine Inertia.—Under this heading RYDER (*Amer. Jour. Obstet.*, September, 1912) describes 18 cases of labor characterized by delay due to poor uterine effort. These 18 cases occurred among 175 labors in private patients. Only 3 of these labors started spontaneously, 14 being induced labors by bags, and 1 an attempted induction by the use of bougies. The patients were near term, 12 multigravidæ and 6 primigravidæ. There was no marked disproportion between mother and fetus. Three cases were delivered normally by high forceps, 5 by medium forceps, 5 by version, 4 of these latter because of complications. There was no maternal mortality, but 5 still-births, and 1 infant death, a total infant mortality of 33.3 per cent. One patient lost 15 ounces of blood, and in 6 others the uterine cavity was packed with gauze to avoid hemorrhage. In 4 the placenta was extracted manually, in 2 part of the membranes; 8 had temperatures above 100.6°. Different methods were used in these cases. In the first 5, when inertia occurred, the effort was made to stimulate the uterus and to finish the labor immediately. The results were so discouraging that this method was discarded. If the membranes were unruptured the patients were left alone, and labor was allowed to start spontaneously. The results were good. In the 5 cases where the effort was made to terminate labor virtually by one operation, 4 of the children were lost. In 9 cases inertia was treated by a waiting method. In the 9 cases where the waiting policy was pursued, many of them had induced labor by the introduction of bags which failed to excite pains. The bag was then removed, when labor subsequently developed spontaneously. In 4 cases the premature rupture of the membranes,

or the persistence of weak pains which destroyed sleep without progress, made it necessary to terminate labor. Primary inertia is especially seen in women, aged over twenty-five years, but more often in patients aged over thirty years. It frequently results from mental conditions only, especially when labor is artificially induced. Rupturing the membranes artificially in primary inertia is a most dangerous procedure. Haste must never be practised, as it exposes the mother to suffering and injury, with a fetal mortality of 80 per cent. In patients where in previous pregnancies and labors there has been inertia, tonics and good hygienic treatment should be used during pregnancy. Labor should not be induced if it can be avoided. It is thought that when labor must be brought on, the dilating bag is less apt to cause rupture of the membranes than the bougie. The membranes should rarely be ruptured, and only when the head is well engaged and the conditions all favorable for delivery. With unruptured membranes, the patient should be left alone, and the nervous system quieted by sedatives until rest can be obtained. With ruptured membranes, there is danger to the fetus, and labor should terminate. Primary inertia is most frequent usually in the first stage of labor, and is not of especial importance in the second and third stages. Postpartum hemorrhage is not especially frequent after primary inertia. When labor has terminated ergot should be given freely, and intrauterine packing used if the uterus does not contract well. Cesarean section is often safer for mother and child in primary inertia than a hard forceps operation or breech extraction. Strychnine, quinine, alcohol, and ergot are not satisfactory in these cases. Pituitrin extract may give better results.

Treatment of Cancer of the Cervix Complicating Pregnancy.—LEVANT (*Archiv mens. l'Obstetrique*, September, 1912) believes that abdominal hysterectomy by Wertheim's method is the operation of choice in cancer of the cervix complicating pregnancy and parturition. It has the advantage of permitting the extraction of the fetus by Cesarean section if the child is viable, while in early pregnancy the uterus may be removed unopened. Vaginal hysterectomy for cancer complicating pregnancy was not satisfactory in his hands, as in 55 cases without Cesarean operation the mortality was 5.4 per cent. These operations were done before, or at the sixth month, and the patient suffered from a return in 31.8 per cent. In 25 vaginal hysterectomies made during the puerperal period, 32 per cent. had a return of the disease in less than one year. The mortality of abdominal hysterectomy by Wertheim's method in cases where cancer complicates pregnancy is considerably less; in the experience of the writer, 16 per cent. during one year; in a subsequent year 18.7 per cent.; then 11.8 per cent.; then 8.6 per cent.

The Treatment of Abortion.—PATEK (*Archiv f. Gynäk.*, 1912, Band xcvi, Heft 1) contributes a paper upon the treatment of abortion in which he analyzes the results obtained by active interference in cleansing the uterus by the curette, with the results obtained by a less vigorous and more expectant method. His conclusions indicate that although fever may be present, the uterus should be emptied

irrespective of all its bacteriological contents, as promptly and thoroughly as possible. Where the patient cannot take ether it may be necessary to secure dilatation by laminary tents, but in the majority of cases etherization and the use of the curette and placental forceps, give the best results.

The Examination of the Blood in Pregnant, Parturient, and Puerperal Patients.—Dor reports from the clinic at Halle (*Archiv f. Gynäk.*, 1912, Band xcviii, Heft 1) the results of his examination of the blood, with especial reference to the toxemia of pregnancy, and the occurrence of eclampsia. He finds that the erythrocytes are somewhat less numerous in pregnant and puerperal patients than in those who are not pregnant. The leukocytes are increased, especially in primiparæ, and increase as labor develops and proceeds. In the first twenty-four hours after labor the leukocytes diminish one-half, and by the fifth day of the puerperal period, are in the normal proportion. This leukocytosis overshadows other conditions in the blood, with the exception of the neutrophile cells. The eosinophile cells and the large cells grow less during pregnancy, disappear during labor, and gradually return during the puerperal period. The index of the neutrophile conditions of the blood is in pregnancy much more developed in parturient patients, and still greater in cases of pregnancy complicated by kidney insufficiency and eclampsia. It returns to the normal in the healthy puerperal period, especially when the albumin disappears from the urine. The blood plates increase in proportion to the leukocytes. In pregnant and parturient women it is not infrequent to see nucleated red blood bodies, microcytes and macrocytes. These disappear during the puerperal period. Changes in the erythrocytes occur more frequently in the kidney of pregnancy than normal, are constant, and are greatly in evidence in cases of eclampsia. The blood changes are much more pronounced in patients having overburdened kidneys during pregnancy than in the normal patient, and these changes are most developed in eclampsia. In infectious disorders the blood changes are in proportion to the virulence of the infection. There is a striking resemblance between the blood changes in pregnancy and those occurring in the blood plates and leukocytes, and reflection of a neutrophile index indicates a predisposition to the formation of thrombi. The blood plates are evidently cells having an important function in blood loss and in the resistance of the organism to toxic material. It is doubtful whether the changes in the leukocytes alone without blood plates, can favor the occurrence of thrombi. From the blood one can gain no knowledge of the actual composition of the toxins present in pregnancy. It is interesting to observe that the least changes in multiparæ with good constitutions, are contrasted with the great changes seen in eclampsia. Primigravidæ having abnormalities have greater blood changes than the normal, and these blood changes are more pronounced in labor than during pregnancy. It is evident that during pregnancy the body is in a condition of very unstable equilibrium, and the changes in the proteid constituents of the body may readily occur and be of very considerable moment.

GYNECOLOGY

UNDER THE CHARGE OF

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Importance of Careful Peritonization After Carcinoma Operations.
—BUMM (*Zentralbl. f. Gyn.*, 1913, xxxvii, 1) believes that most careful and thorough covering with peritoneum of all raw areas left after any operative procedure is of the greatest importance, but especially is this true after the radical abdominal operation for carcinoma of the uterus. In his own experience, the effect of a gradual adoption of this principle with corresponding reduction in the amount of drainage used, has been well shown by the coincident steady fall in his mortality. His worst results from this operation were obtained when he routinely drained the pelvic cellular tissue by means of gauze packs brought out through the vagina, the mortality of 138 cases operated on in this manner being nearly 30 per cent. In almost a third of the cases suppuration and sloughing occurred in the tamponed cavities, with resulting necrosis of the peritoneum over them, and ascending peritonitis. Somewhat better results were obtained after he abandoned gauze drainage of the cellular tissue, uniting the loosened bladder and rectum with the edges of the vagina, and closing the raw areas in the broad ligaments on each side with a running suture. Even with this technique, however, he could not get away from the idea of drainage completely, but now placed the drain in the lower angle of the pelvic peritoneum, still bringing it out through the vagina. During this epoch his mortality was 21 per cent., most of it due as before, to ascending peritonitis. All this has been changed, however, since omitting drainage of any sort. Bumm's technique at present is to close all raw surfaces from the free peritoneal cavity by means of a double layer of sutures, the first uniting the edges of the peritoneum, and the second reinforcing these by folding it over a little more, on the same principle that two layers of sutures are placed around any intestinal opening. By following out this technique, Bumm has reduced his mortality in his last 100 cases to the remarkably low figure of 6 per cent., a result which he ascribes solely to the improved method, as the cases were in all respects similar to those of the earlier series. He thinks that the gauze drain only serves to collect wound secretion, which forms an excellent culture medium for the pathogenic organisms which are always present in carcinomatous tissue. When, however, the peritoneum is carefully closed at all points, leaving nothing but a smooth surface, in which no raw areas are to be seen, it is able to take care of considerable quantities of even highly virulent organisms, and to destroy them. One point of importance when following out this technique, however, is to avoid as far as possible spreading infection from the carcinomatous area during the operation, and also never to operate on these patients while they are running a temperature even slightly above normal.

Is Hysteria Ever a Justifiable Diagnosis in Gynecology?—In view of the tendency, which is of late becoming manifest, to ascribe many symptoms apparently referable to the female genital system to psychic disturbances alone, SIPPEL (*Deutsch. med. Woch.*, 1913, xxxix, 263) thinks that a word of warning is in place. Many such cases, especially if no definite pathological condition can be made out by the ordinary examination, are put down as "hysteria," a diagnosis which in the vast majority of cases not only expresses the inability of the attending physician to discover the real trouble, but carries with it two unfortunate sequelæ—failure to relieve the patient of real distress, and the transformation of an originally nervously sound woman into a true neurasthenic because of this failure, and of the knowledge that she is being wrongly judged. Sippel urges that the diagnosis "hysteria" should never be made until most careful and repeated examinations have failed to reveal any demonstrable local lesion, and that even then the possibility of a purely psychic origin of definite pain should be regarded with much skepticism, believing rather that most of these cases merely indicate our inability always to diagnosticate minor anatomical changes. A most useful method of arriving at the true diagnosis in many of these cases has been, in his experience, to have the patient anesthetized merely to the point where sensibility and the ordinary reflexes are just barely lost. If now a reflex can be elicited by pressure on the region complained of by the patient, proof is furnished that an actual physical lesion exists. In cases of a somewhat different category—where a tumor can be felt in the pelvis, but its origin cannot be determined—the employment of the exaggerated Trendelenburg position, in addition to light narcosis, may be of the greatest help. Under these conditions, adnexal tumors will fall sufficiently away from the uterus to be easily differentiated from it, even though with the patient in the ordinary position on the examining table this may have been impossible.

Postoperative Infection of the Urinary Tract.—In order to determine by what routes pathogenic organisms most commonly reach the bladder and upper urinary tract after operation, BAUEREISEN (*Zeitschr. f. gyn. Urologie*, 1913, iv, 1) has made an examination of the organs removed at autopsy from 18 postoperative cases, the majority of these having been Wertheim operations for carcinoma of the cervix. He has found that organisms reach the bladder, in the vast majority of cases, through the urethra, either by spontaneous ascension, or as the result of catheterization. In a few instances, organisms may get to the bladder by way of the blood current, after passing the kidneys; this is especially true of colon bacilli. In the urethras of normal women, not confined to bed, staphylococci are always present, and colon bacilli in 60 per cent.; in bed patients, the colon bacillus also is present in all cases. After a radical cancer operation, the secretion from the wound cavity, rich in pathogenic organisms, flows out through the vagina past the urethral orifice, so that the urethra becomes abnormally rich in bacteria, and it is in this way that they get into the bladder. Only very rarely, apparently, does direct propagation or transportation through the vesical wall take place, this being prevented by the wall of inflammatory tissue that forms in its outer portion, and also by the

adverse lymph current. Infection of the ureter usually occurs in a similar manner—by direct ascension through the lumen, aided perhaps by postoperative over-distention of the bladder. The same factors prevent the transmission of organisms through the ureteral as through the vesical wall. The kidneys are infected most commonly by ascension through the ureter, less frequently through the blood current. In the latter cases the organisms originate from the operative area, not from the intestine, becoming scattered into the blood during the operation, and then partially excreted by the kidney. Of the organisms which may infect the kidney in this manner, the staphylococcus is unquestionably the most dangerous. Once the renal cortex is involved, the organisms may spread to the capsule and cause a perinephric infection. For the fatty capsule, still another mode of infection must be taken into consideration, however, the lymph channels in the connective tissue along the ureters from the true pelvis to the kidneys. Infection by this route causes a perinephritis, which may spread secondarily to the kidney substance.

Influence of Myomas on the Blood Supply of the Uterus.—In continuation of some studies into the blood supply of myomas themselves, published about a year ago, SAMPSON (*Surg., Gyn., and Obst.*, 1913, xvi, 144) now reports the results of his investigations into the effect that the presence of such tumors has upon the circulation of the uterus. The method pursued in both these lines of investigation has been to inject large numbers of myomatous uteri with various substances, in some cases using colored gelatine masses, red for the arterial system, blue for the venous, in others, radio-impenetrable substances, and then to make slices of the organs in various directions, studying these by direct inspection and by means of radiographs. Sampson has found that small and moderate-sized subserous myomas (up to 10 cm. in diameter) do not disturb the uterine circulation, and do not alter menstruation. Larger subserous tumors may produce marked enlargement of the branches of the uterine artery from which they derive their nourishment, and may also give rise to large venous channels in their pedicle and in the peripheral zone of the uterus, but the "radial zone," immediately surrounding the endometrium, which is normally anemic, remains unaffected. There is therefore no excessive escape of blood into the uterine cavity in these cases, and menstruation in them also is unchanged. Occasionally, however, the large venous channels in the pedicle become injured by movements of the tumor, and give rise to hemorrhage into the peritoneal cavity. Intramural myomas do not appear to alter the arterial blood supply of the uterus to an appreciable extent, unless present in very large numbers, in which case the uterine arteries may be somewhat enlarged. The venous plexus of the myometrium may show about the tumors a localized, or even a general dilatation, varying with their size, and when the myomas are very numerous there may be an increase in the thickness of the uterine wall, due to an actual hypertrophy of the myometrium, to a dilatation of the venous plexus, or to a combination of both these factors. Such tumors do not greatly interfere with the circulation of the uterus, and do not usually alter menstruation, although they may indirectly cause menorrhagia or metrorrhagia, the factor of muscular

insufficiency probably playing an important role in these cases. Intramural myomas which encroach on the uterine cavity cause an atrophy and anemia of the mucosa immediately over them; the remaining endometrium is usually hypertrophied, and its venous plexus more dilated than normal. It is from this portion of the endometrium, and not from that encroached upon by the tumors, that the menstrual flow occurs. When excessive hemorrhage takes place in these cases, it is probably due to failure of the uterine muscle to control properly this excessive amount of venous blood, and to a slow regeneration of the endometrium. Occasionally dilated veins in the endometrium over the tumor may become eroded, and give rise to bleeding, but this is not very common. Submucous myomas represent merely a later stage of the intramural variety; the veins over the surface of these are more exposed to injury or degeneration than with intramural tumors, but even here the source of profuse menstruation is usually the portion of the endometrium not encroached upon.

DERMATOLOGY

UNDER THE CHARGE OF

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Cosmetic and Toilet Powders.—KAPP (*Dermat. Woch.*, 1912, No. 16) concludes that the vegetable powders always injure the skin in a mechanical way through the swelling of the granules in the follicles. Rice powder is the least injurious, as it swells the least. Concerning mineral powders the sharp edges of the crystals of some of them may injure the skin. Zinc oxide, precipitated magnesium carbonate, and magnesium silicate being the least objectionable. Bacteriological examinations go to show the possibility of the transmission of various diseases by means of powder puffs and the like.

Noguchi Luetin Reaction in Dermatology.—D. O. ROBINSON (*Jour. Cutan. Dis.*, August, 1912) states that luetin is the extract prepared from pure cultures of the *Spirocheta pallida*, and is intended for use in the diagnosis of syphilis as von Pirquet's test is for tuberculosis. Noguchi informs us that the extract of the *pallida*, which he designates "luetin" does not produce any marked inflammation in the skin of non-syphilitics, while it gives a definite lesion formation in most cases of tertiary, latent, and late hereditary syphilis. Robinson's conclusions are in effect that the luetin reaction was found to be specific for syphilis and affords a means of diagnosis in certain cases.

It was absent in primary and secondary untreated cases. It was present in all cases of tertiary, latent, and late hereditary syphilis in the cases reported, and in these forms of the disease was more constant than the Wassermann reaction.

Organism Found in Leprosy.—DUVAL and WELLMAN (*Jour. of Cutan. Dis.*, July, 1912), from "a critical study of the organisms cultivated from the lesions of human leprosy, with a consideration of their etiological significance," arrive at the following conclusions: Out of 29 cases of leprosy in Louisiana, Duval and Wellman found an acid-fast bacillus in 22 cases. A chromogenic strain similar in all essentials to that described by Clegg was recovered in 14 cases, which under certain conditions grows as (1) non-acid-fast streptothrix, (2) non-acid-fast diphtheria, and (3) an acid-fast bacillus. The role played by the bacillus of Clegg in the production of leprosy is an unsettled question. The wide variation in morphology and staining reaction would go to show that the *Bacillus lepræ* is one of pleomorphism.

High-frequency and High-tension Currents in the Treatment of Certain Skin Diseases.—A. FONTANA (*Dermat. Woch.*, May 4 and 12, 1912) refers to many cases of diverse disease in which these currents were employed over a period of several years, used in the form of effluve, brush electrode, condensation electrode, and sparking, with the view of obtaining soothing effect (*e. g.*, in pruritus, eczema, etc.), revulsive effect (*e. g.*, in alopecia areata, etc.), decongestive effect (*e. g.*, in acne, wart, lupus, etc.), reparative effect (*e. g.*, in atonic ulcerations, etc.). Perhaps the best results were obtained from the effluve, but these were not uniformly favorable. On the whole, the results were not entirely satisfactory.

Generalized Iodine Acne and Macular Exanthem following the Application of Tincture of Iodine.—HODARA (*Dermat. Woch.*, 1912, No. 10) reports the following unusual iodine eruption: A man, aged sixty-seven years, applied tincture of iodine on three successive days to painful areas following intercostal neuralgia, and covered it with oil-cloth. Some days later an eruption suddenly appeared, consisting of acne-like papules with small pustules upon the tops, surrounded by a red halo. This eruption spread over the whole body, covering the face and head, and in a less degree the trunk and extremities. Upon the limbs and the trunk there was also a macular eruption consisting of round and irregularly-shaped macules. There was no fever or other constitutional disturbance. On account of its resemblance to variola some of Hodara's colleagues were inclined to regard the eruption as either varioloid or varicella. In connection with this case reference may be made to another one recently reported by GOODALL (*British Jour. Dermat.*, June, 1912), in which a varioliform eruption followed the internal administration of ferrous iodide.

The Influence of Milk Fat on the Skin.—MONTGOMERY and CULVER (*Jour. Cutan. Dis.*, June, 1912) in a short but most interesting paper on the influence of fats of various kinds, especially the fats derived from milk, upon the skin, express the opinion that the ingestion of

large quantities of butter or other fats obtained from milk increases very much the difficulties of successfully treating seborrhea and seborrheic affections. While they do not believe that the quality and quantity of fat taken acts as a poison, they do believe that it lowers the resistance of the skin and increases its susceptibility to attack by bacteria of various kinds, making the patient more liable to acne, seborrheic eczema, furuncle, carbuncle, and erysipelas.

The Etiology of Lupus Erythematosus.—FRESHWATER (*British Jour. of Dermat.*, February, March, 1912) does not think there is sufficient evidence, clinical, histological, or bacteriological, to prove that lupus erythematosus is always a tuberculous lesion. The hypothesis that it is due to a tuberculous toxin in the blood is far from satisfactory, since there are numerous cases in which there are no signs of tuberculosis. The fact that it sometimes follows a local injury to the tissues, such as frost-bite, sunburn, etc., strongly suggests that it may occasionally be due to purely local causes. Since a large proportion of cases of erythematosus lupus suffer from some anomaly of the circulation, Freshwater thinks the skin is, on that account, less able to tolerate the effect of toxins circulating in the blood, and therefore more liable to disease. The primary implication of the blood-vessels, and the symmetrical arrangement of the disease in the majority of cases, favors the theory that the causal agent acts through the blood. He concludes that erythematosus lupus is probably brought about by some injury to the skin in an individual with a feeble circulation, to which may be added some toxin circulating in the blood.

Granuloma Pediculatum (So-called Human Botryomycosis).—HEUCK (*Dermat. Zeitschr.*, March, April, May, 1912), from a recent study of the so-called human botryomycosis, concludes that this affection, which is identical with the granuloma telangiectaticum of Kütner, is a well-defined form of disease, for which he proposes the name "granuloma pediculatum," dropping that of botryomycosis. According to its histological structure it may be divided into two groups: (a) granuloma pediculatum simplex, which is essentially composed of granulation tissue with an inclination to dilatation of the vessels and proliferation of the endothelium and the perithelial spindle cells; (b) granuloma pediculatum angiomatosum, which shows the same structure, but with an inclination to the formation of excessively large blood-spaces and well-marked foci of spindle cells. From its structure, seat, and benign character it may be concluded that it is a simple inflammatory granuloma which arises from trauma and infection. It is distinguished, however, from simple granulation tissue by the marked tendency to dilatation of the vessels, the inflammatory proliferations, and the perivascular collections of spindle cells which may be so considerable as to resemble sarcoma. The etiology of granuloma pediculatum is yet unknown; that the *Staphylococcus pyogenes aureus* plays a role in its production has not yet been proved. It seems in the highest degree probable that it arises from some external infection. Heuck believes (as most of those who have recently studied the affection) that it is not identical with the botryomycosis of animals.

The Etiology of Impetigo Contagiosa.—K. DOHI and SH. DOHI (*Archiv f. Dermat. u. Syph.*, 1912, Band cxi, Heft 2), as the result of their study of impetigo contagiosa, conclude that there are two forms which are clinically and etiologically different. The first form is distinguished clinically by the formation of vesicles and blebs with clear, later cloudy, contents which leave thin crusts. In the contents of the lesions as well as in the surrounding skin white staphylococci may always be demonstrated. The second variety is characterized by the formation of wax-yellow thick crusts, and in the lesions of this form which become pustules, streptococci are always present. When yellow staphylococci are present in either form it is as the result of secondary infection. The first form, that due to the white staphylococci, frequently occurs epidemically in small children and only in the warm season of the year, while the second variety occurs sporadically at all seasons, in adults as well as children, but mostly in young people.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Life-cycle of Spirochetes.—Much interest has lately been aroused in the supposed life-cycle of *Spirochaeta pallida* which has been discovered in a complete series of phases. E. H. ROSS (*British Med. Jour.*, December 14, 1912) publishes a short paper indicating his understanding of the process, but we regret to say that priority cannot be given to him until there is a satisfactory answer to the letter of J. E. R. McDONAGH, of the London Lock Hospital, published in the *British Medical Journal* of December 21, 1912, for in this letter the latter states that the discovery is his own, and that he has given his colleague, Dr. Ross, material which showed the life-cycle, without any acknowledgement of the same having been made. It may be recalled that de Korte, in the *Practitioner* for June, 1906, described cyst-like bodies containing crystalline threads, in the chancres of syphilitic patients. Study by the jelly method of staining (*in vivo*) with borax methylene blue serves to show the parasites, which appear as copper-colored bodies, either free or ameboid, or enclosed in mononuclear cells. In the copper-colored cytoplasm are granules, and a nucleus which appears as a clear space with a black, dotted centre; should the parasite die, the sphere becomes colorless; 143 cases of preliminary and secondary syphilis have been examined, and the intracellular and extracellular bodies have been found in every case; they have been so found in chancre, in non-suppurative lymph nodes, in the blood from maculae and condylomas, in ulcerating tonsils,

and in the peripheral blood. Ross considers that these round or pear-shaped bodies, originally free, become included in the cytoplasm of various kinds of cells; here they surround themselves with a wall. Growth proceeds and the chromatin divides. The chromatin within the parasites stains deeply in masses, and these masses vary in number from one to twelve. While still within the cell, in some cases, the chromatin mass, when it has reached full size, gives origin to several minute curled and twisted threads which closely resemble *Spirochete pallida*. Ross sees a parallel to the intercellular parasites found in guinea-pigs and earth-worms; he has failed so far to find these bodies in non-syphilitic cases. The suggestion is that the spirochetes are really microgametes or male elements, and that some of the round or pear-shaped bodies are possibly macrogametes or female elements. In the same number of the *British Medical Journal* appears a paper by E. JENNINGS, who has used the jelly method and found the same bodies as are here mentioned; while S. R. MOOLGAVKAR, still in the same number, describes similar bodies.

Thyroid Action and Reaction.—FARRANT (*Proc. Royal Soc. Med., Path. Soc.*, London, 1912, vi, 21) points out that there has been a general recognition among pathologists that the histological appearance of the thyroid is apt to be modified in sundry cases of infection. Hitherto, to our knowledge, no one has carefully studied this matter, so that Farrant's observations here given appear so novel as to demand confirmation. Nevertheless the fact that they emanate from Prof. Cushing's laboratory is in itself strong evidence in favor of their immediate acceptance. Farrant points out that the thyroid secretion reaches the circulation by means of the veins, that absorption occurs by the lymphatics is now known to be erroneous. The inferior thyroid veins are the largest, and more than two-thirds of the thyroid secretion reaches the left side by means of the thyroid veins. The left innominate vein receives the thoracic duct, the right, the right lymphatic trunk. Thus there is a correspondence between the opening of the thyroid veins and of the lymphatic trunks, and it may well be asked whether the thyroid has any influence upon the destruction of toxins reaching the venous system through the main lymphatics. Farrant illustrates by numerous photographs that in cases of infantile diarrhea, diphtheria, measles with bronchopneumonia, and whooping cough with bronchopneumonia, according to the duration and intensity of the disease, so does the thyroid present evidence of a succession of changes which can only be regarded as indicating increased production and discharge of secretion. He notes the following succession of changes: (1) The colloid becomes finely granular; (2) it becomes vacuolated and partially absorbed; (3) the cells lining the vesicles become more numerous, elongated, approaching the columnar type and arranged in masses; then the colloid becomes entirely absorbed, becoming crenated and infolded; (4) the infolding and cell increase tend to transform the vesicles into solid masses of cells. He next proves from experiment that this thyroid reaction is caused by the toxins, finding the same succession of changes to occur in the thyroids of guinea-pigs which have been injected with diphtheria toxin, and he is able to show that when the guinea-pigs injected with diphtheria toxin

are simultaneously given thyroid powders, there is a marked delay in the fatal event, so much so that guinea-pigs, previously fed on thyroid, in several cases survived when given one and a half times the minimal lethal dose. These findings led to a further series of observations in which it was discovered that blood serum of the thyroid fed animals gains definite antitoxic properties. Of the 5 guinea-pigs which had been so fed, 4 survived one and one-half times the minimal lethal dose of diphtheria, whereas all the controls died in from two to six days. The one exception died with an abscess developing in the neck. It is further noted that rabbits fed with diphtheria toxin developed the same symptoms as those produced by thyroid feeding, namely, loss of weight, tachycardia, fur changes, etc., while diphtheria antitoxin fed to thyroidectomized animals in similar quantities has no ill results; on the contrary, there is a distinct gain in weight. Lastly, it is found that in horses employed in the production of diphtheria antitoxin, the serum contains much more iodine than does that of the normal animal. From this it is concluded that certain toxins stimulate the thyroid into a condition of hyperplasia; during this change it seems probable that iodine-containing substances are poured out into the circulation. This indicates some close relationship between thyroid function and the development of certain antitoxins, and it is suggested that the hyperplasia observed in the condition of toxemia above noted is intimately associated with the attempt to form antitoxins. The article is illustrated with 30 good microphotographs of sections of thyroid in various conditions—cases of the disease as above noted, from horses treated with diphtheria toxins, and from guinea-pigs similarly treated.

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NEPHRITIC HYPERTENSION: CLINICAL AND EXPERIMENTAL
STUDIES.¹

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WHEN Richard Bright,² in 1836, published his "Cases and Observations Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine," he set in motion an inquiry that has been unrestingly pursued during the past three-quarters of a century, and that is today still far from its goal. This inquiry concerns the phenomenon of high arterial pressure in man and its relation to chronic disease of the kidneys. In this now famous paper, Bright gave the results of his clinical study of one hundred patients, compared with the findings at autopsy. His study revealed a coincidence of cardiac and renal disease so striking as to convince him that the disease of the heart must be regarded as the result, more or less direct, of the disease of the kidneys. He comments upon the relationship in these words:

"The deviations from health in the heart are well worthy of observation: they have been so frequent, as to shew a most important and intimate connection with the disease of which we are treating; while at the same time there have been twenty-seven cases in which no disease could be detected; and six others, which,

¹ Read before the Harvey Society, New York, February 15, 1913, and the Rush Society, Philadelphia, March 14, 1913.

² Cases and Observations Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine, Guy's Hospital Report, London, 1836, i, 338.

from not having been noted, lead to the belief that no important deviation from the normal state existed. The obvious structural changes in the heart have consisted chiefly of hypertrophy, with or without valvular disease: and, what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four: . . . This naturally leads us to look for some less local cause, for the unusual efforts to which the heart has been impelled: and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation, as to render greater action necessary to force the blood through the distant subdivisions of the vascular system."

I ask you to note particularly two things: (1) While Bright was convinced that he had discovered a real relationship between pathologic processes in distant organs, he made no attempt to blink the fact that this relationship is by no means a constant one; (2) he did not speculate beyond certain broad inferences which, to his sane and clinically trained mind, seemed warranted by the facts themselves. These inferences were, that the hypertrophy of the heart must be attributed to unusual work performed by that organ, and that the cause of the unusual work must lie either in unwonted, direct stimulation of the heart or in heightened peripheral resistance. Either condition, it seemed to him, could be attributed to an altered quality of the blood, associated with the disease in the kidneys. That these suggestions contained the germ of such subsequent explanations of the phenomena as have attained to any wide acceptance, bears witness to the insight into disease processes which may be gained by the attentive study of clinical symptoms in connection with the concomitant anatomical lesions. It is an insight which in the history of medicine has usually recognized its own limitations. The contrast between such modes of thought and some of the more recent speculations on the same subject is apparent.

I. THEORIES AND EXPERIMENTS. For fifty years after Bright the origin of the cardiac hypertrophy found in kidney disease was a favorite theme of pathologists. It was the subject of extensive anatomic investigations and considerable experimental study. With the invention of the first clinical instrument for measuring blood pressure, by von Basch in 1876, the way was opened for fuller investigation of the physiology of the circulatory disorder of which the pathologist saw the end result. Since reasonably accurate instruments were brought forward in 1896 by Riva-Rocci and by Hill and Barnard, and the sphygmomanometer has been generally adopted in medical practice, the point of attack on the problem has shifted, so that at the centre of our inquiries today stands nephritic hypertension.

These two problems of nephritis, the cause of the high blood pressure and the cause of the hypertrophied heart, must not be identified absolutely. In the main, however, the hypertrophied heart may be looked upon as the result of a persistently high blood pressure. To this point of view practically all authorities are now committed. The evidence for this statement is well formulated by Krehl³ and by Jores.⁴ Such ideas as those of von Bühl,⁵ that the hypertrophy is dependent upon inflammatory processes in the heart itself, have never had wide acceptance. Even Senator,⁶ who in 1902 laid some stress on the first suggestion of Bright, that is, primary stimulation of the heart, as a factor at least in the hypertrophy found in so-called chronic parenchymatous nephritis, did not recur to this point of view in his last review of the subject.⁷ Schlayer⁸ has reported a few instances in which cardiac hypertrophy apparently preceded a rise in pressure. I, too, have seen young people in whom the heart seemed enlarged while the blood pressure remained within normal limits. In the normal animal, with intact vagus and vasomotor mechanisms, a long maintained high blood pressure is prevented automatically. It is also a common clinical observation that high arterial pressure persists even in patients with markedly incompetent hearts, the condition called by Sahli "Hochdruckstauung." I⁹ have always been convinced, therefore, that the hypertrophy of the heart cannot explain the high blood pressure of nephritis, though it may be one contributing element. Krehl,¹⁰ in the last edition of his book, also insists on this. Hence, I shall confine the present discussion of the problem to nephritic hypertension, using the word "nephritic" for the sake of brevity, not in any strict sense, but to indicate only association with disease of the kidneys. Until pathologists can all agree upon the diseases of the kidney which they will consider inflammatory and entitled to the designation "nephritis," clinicians may be pardoned for saving the time of their audiences by a loose use of terms.

While I shall present mainly the results of the newer clinical and experimental studies upon the subject, due weight must be given to the mass of anatomic evidence as to the relative frequency

³ Pathologische Physiologie, Leipsie, 1912, 7th edition, pp. 36 and 37.

⁴ Ueber die Beziehungen der Schrumpfnieren zur Herzhypertrophie vom pathologisch-anatomischen Standpunkt, Verhandl. deutsch. path. Gesellsch., 1908, xii, 187 (see editorial, Jour. Amer. Med. Assoc., 1909, lii, 565); Deutsch. Arch. f. klin. Med., 1908, xciv, 1.

⁵ Ueber Bright's Granularschwund der Nieren und die damit zusammenhängende Herzhypertrophie, Mitteil. aus dem Path. Institut zu München, 1878, p. 38.

⁶ Die Erkrankungen der Nieren, Vienna, 1902, pp. 110-129.

⁷ H. Senator, Ueber die Beziehungen des Nierenkreislaufs zum arteriellen Blutdruck und über die Ursachen der Herzhypertrophie bei Nierenkrankheiten, Zeitschr. f. klin. Med., 1911, lxii, 189.

⁸ Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med., 1911, cii, 3 and 4, 323.

⁹ Theodore C. Janeway, The Clinical Study of Blood Pressure, New York, 1904, p. 142.

¹⁰ Pathologische Physiologie, Leipsie, 1912, 7th edition, p. 37.

of cardiac hypertrophy in the various types of nephritis. A theory of nephritic hypertension must be adequate to explain the underlying anatomic facts as well as the varied behavior of the blood pressure during life, including its response to therapeutic measures. It must be in accord with the recognized physiologic laws governing the circulation. The problem, however, is set by the clinical facts, and it should be borne in mind that permanent hypertension is a human pathologic phenomenon, which has no counterpart in the realm of normal animal physiology thus far investigated.

MECHANICAL THEORIES. The only theory which has sought to explain the hypertension of nephritis on different lines from those suggested by Bright has been the purely mechanical theory first advocated by Traube¹¹ and elaborated by Cohnheim.¹² In its original form it sought to explain high pressure by increased peripheral resistance in the kidney itself. This theory was disproved by the observation that ligature of both renal arteries fails to raise the blood pressure. It has recently been resurrected in modified form by Katzenstein,¹³ who claimed to get a slight rise in blood pressure after incomplete occlusion of the renal vessels and after temporary complete occlusion, by which he claimed to produce thrombosis of the smaller renal arteries. There was a rise in the blood pressure of the animal when the circulation was reestablished. Further experiments in this direction, made by Müller and Maas,¹⁴ who embolized the kidney extensively with paraffin, failed to demonstrate a rise in blood pressure. Alwens,¹⁵ also, does not confirm Katzenstein's observations, but he was able to produce small rises in blood pressure by compressing the kidneys in occometers, using an amount of external pressure approximating or surpassing the aortic blood pressure. The same amount of pressure applied to the lower extremities was without influence. Alwens himself admits that the rise in pressure obtained under these conditions is too slight, as compared with the hypertension of nephritis, to suggest that the mechanical factor is more than subordinate in the production of human high blood pressure. He admits also that the mechanism is purely passive, the actual transmission of the pressure exerted upon the kidney out through the renal artery to the aortic blood column. Such a procedure, as Senator¹⁶ remarks, can have no counterpart in human pathology, where the only source of pressure available is the existing aortic blood pressure.

¹¹ *Gesammelte Abhandlungen*, Berlin, 1856, ii, 290; iii, 440.

¹² *Vorlesungen über allgemeine Pathologie*, Berlin, 1880, ii, 355.

¹³ *Experimenteller Beitrag zur Erkenntnis der bei Nephritis auftretenden Hypertrophie des linken Herzens*, Virchow's Arch. f. path. Anat., 1905, clxxxii, 327.

¹⁴ H. Senator, Ueber die Beziehungen des Nierenkreislaufs zum arteriellen Blutdruck und über die Ursachen der Herzhypertrophie bei Nierenkrankheiten, *Zeitschr. f. klin. Med.*, 1911, lxii, 189.

¹⁵ Experimentelle Untersuchungen über die Bedeutung der mechanischen Theorie der nephritischen Blutdrucksteigerung, *Deutsch. Arch. f. klin. Med.*, 1910, xeviii, 137-163.

¹⁶ Ueber die Beziehungen des Nierenkreislaufs zum arteriellen Blutdruck und über die Ursachen der Herzhypertrophie bei Nierenkrankheiten, *Zeitschr. f. klin. Med.*, 1911, lxii, 189.

A theory which can in part be interpreted as mechanical was propounded by Loeb.¹⁷ It was based upon the claim that the anatomic study of nephritics showing hypertension brought out a parallelism between the extent of glomerular changes and the height of the blood pressure. Upon this finding was based the theory that the hypertension of nephritis should be considered in the nature of a regulatory function, probably evoked reflexly, in order to provide an adequate flow of blood through the kidney, when local vasodilatation within that organ was no longer sufficient, because of capillary obliteration in the diseased glomeruli. The anatomic basis of Loeb's theory has been destroyed by Jores¹⁸ in a careful study of serial sections taken from the kidneys of four subjects. The two who had shown the highest blood pressure and the most marked cardiac hypertrophy had the least extensive glomerular lesions. He also cited one instance where the heart was markedly hypertrophied and the kidneys showed scarcely recognizable histologic changes. Certainly no one who has had the opportunity to observe a large series of autopsies on nephritic individuals can fail to agree with Jores, that there is no strict parallelism between glomerular changes and blood pressure. While it seems clear that the types of nephritis most regularly characterized by hypertension are characterized equally by extensive glomerular lesions, it is also evident that there exist, as Bright observed and as all subsequent statistics have shown, many instances of extreme glomerular nephritis without cardiac hypertrophy.¹⁹ The most fatal objection to a purely glomerular theory of hypertension lies in the fact that amyloid disease, which is *par excellence* a disease of the glomeruli, in its pure form is almost invariably without effect on the blood pressure, and without an accompanying hypertrophy of the heart. This fact is one of the most difficult to be reconciled with any theory of nephritic hypertension.

CHEMICAL THEORIES. The germ of the many chemical theories, as we have seen, lies in Bright's suggestion that altered composition of the blood is the probable cause. Johnson²⁰ first elaborated

¹⁷ Ueber Blutdruck und Herzhypertrophie bei Nephritikern, Deutsch. Arch. f. klin. Med., 1905, lxxxv, 348.

¹⁸ Ueber die Beziehungen der Schrumpfnieren zur Herzhypertrophie vom pathologisch-anatomischen Standpunkt, Verhandl. deutsch. path. Gesellsch., 1908, xii, 187 (see editorial, Jour. Amer. Med. Assoc., 1909, lii, 565); Deutsch. Arch. f. klin. Med., 1908, xciv, 1.

¹⁹ Von Bühl (Ueber Bright's Granularschwund der Nieren und die damit zusammenhängende Herzhypertrophie, Mitteilungen aus dem Path. Institut zu München, 1878, p. 57) extremely contracted kidneys without enlargement of the left ventricle, 7.9 per cent.; Potter (Cardiac Hypertrophy as Observed in Chronic Nephritis; Russell Sage Institute of Pathology Statistics, Jour. Amer. Med. Assoc., 1906, xlvii, 1351) 66 cases of chronic interstitial nephritis, no hypertrophy, 58 per cent. (a large number of these were in aged or greatly debilitated individuals, and the estimate of hypertrophy was not by Müller's method of weighing); von Bamberger (Ueber Morbus Brightii und seine Beziehungen zu anderen Krankheiten, Samml. klin. Vorträge, No. 173, September 3, 1879) 807 cases of primary Bright's disease, enlargement of the heart in 344, or 42.6 per cent.; Hirsch (Ueber die Beziehungen zwischen dem Herzmuskel und die Körpermuskulatur, und über sein Verhalten bei Herzhypertrophie, Deutsch. Arch. f. klin. Med., 1899, lxiv, 597; 1900, lxxviii, 55, 321), weighing by Müller's method, small material, 72 per cent.

²⁰ The Pathology of the Contracted Granular Kidney, London, 1896.

this suggestion into the conception that accumulated waste products due to failure of the excretory function of the kidney cause vasomotor spasm and later hypertrophy of the muscular coats of the arteries. The older experimental work along this line gave inconclusive results. Excision of a single kidney was without clear-cut effects, and double nephrectomy led to too rapid death for cardiac hypertrophy to develop. Recent experiments by Mosler,²¹ in which thirteen rabbits survived the removal of both kidneys for forty-eight hours, showed a rise in the carotid blood pressure of all the animals but two, the rise being over 15 mm. in four and 25 mm. in one. Real insight into the problem of the complex changes accompanying quantitative renal insufficiency was first afforded by the admirable studies of Tuffier,²² and especially of Rose Bradford.²³ The latter excised one kidney in a large series of dogs, and watched the effect of removing successive portions of the remaining kidney. Bradford discovered that the removal of three-quarters of the total kidney substance resulted in death by emaciation and asthenia in from one to six weeks. The removal of two-thirds often resulted similarly; but if less than two-thirds were taken out, the animal showed practically no serious disturbances. His findings have been corroborated by Pearce²⁴ and his coworkers, who have improved upon the methods and have made valuable studies of nitrogen metabolism in such animals. Pearce occasionally was able to remove even three-quarters of the kidney substance in dogs without producing serious symptoms. It is clear then that for dogs the "factor of safety" in the kidney, in Meltzer's²⁵ sense, is approximately two-thirds, and the indispensable amount of kidney substance required by the animal not over one-third. Animals with these extreme reductions in kidney substance, which may be considered analogous to advanced kidney atrophy in man, developed early and marked polyuria.

In 1905 Pässler and Heineke²⁶ applied this method to the problem of hypertension: They argued that as high blood pressure is most common in individuals with contracted kidneys it was reasonable to suppose that some relation between blood pressure and amount of functioning kidney tissue would be disclosed. They performed successive reductions of kidney substance in 18 dogs, of which 7

²¹ Ueber Blutdrucksteigerung nach doppelseitiger Nierenextirpation, *Zeitschr. f. klin. Med.* 1912, lxxiv, 297 to 302.

²² *Etudes expérimentelles sur la chirurgie des reins*, Paris, 1889 (quoted by Rose Bradford).

²³ The Results Following Partial Nephrectomy and the Influence of the Kidney upon Metabolism, *Jour. Phys.*, 1899, xxiii, 415.

²⁴ The Influence of the Reduction of Kidney Substance upon Nitrogenous Metabolism, *Jour. Exp. Med.*, 1908, x, 632. A Study of Experimental Reduction of Kidney Tissue, with Special Reference to the Changes in that Remaining, *Jour. Exp. Med.*, 1908, x, 745.

²⁵ The Factors of Safety in Animal Structure and Animal Economy, Harvey Lectures, Philadelphia, 1906-1907, p. 139.

²⁶ Versuche zur Pathologie des Morbus Brightii, *Verhandl. d. deutsch. path. Gesellsch.*, 1905, ix, 99.

lived longer than four weeks without severe cachexia. On 5 of these dogs they made satisfactory blood-pressure observations by taking readings from the femoral artery before operation, eight days after operation, and several weeks after the last operation. These dogs showed an average increase in the blood pressure of 21.5 mm., the maximum increase being 29 and the minimum 15 mm. If too much tissue was removed a cachectic state ensued and the blood pressure fell. These 5 dogs also showed well-marked hypertrophy of the left ventricle as compared with the right. For all 7 dogs the average proportionate weight of the left ventricle to the right showed an increase over the normal of 28.5 per cent. These dogs quite regularly developed polyuria before the rise in blood pressure occurred. No reasonable criticism can be urged against these experiments. Pässler,²⁷ in a review of the whole subject, based on his experiments and clinical studies, concludes (1) that the hypertrophied heart in nephritis is the consequence of the kidney disease; (2) that as a result of the kidney lesion there probably occurs an increased irritability of the vasoconstrictor apparatus, in consequence of which arise arterial spasm and increase of resistance in the aortic circulation; (3) that the hypertrophy of the left auricle and of the right heart in nephritis is a later consequence of insufficiency of the left ventricle. This he argues not only from the finding of pure left ventricular hypertrophy in his experiments but from a critical review of the clinical evidence, which seems to me satisfying.

Formerly, hypertrophy of the entire heart, right as well as left, frequently found in the extensive postmortem statistics, seemed a serious obstacle to the acceptance of any theory which sought to explain the hypertrophy on the basis of increased resistance in the aortic circulation. Krehl, in the earlier editions of his *Pathologische Physiologie*, was strongly impressed with the difficulty of explaining this right ventricular hypertrophy. Many attempts were made to discover factors which would influence equally the right and the left heart. Increased viscosity of the blood, for instance, was postulated until clinical studies showed that this did not usually exist in hypertensive nephritis.²⁸ There is a small but interesting group of patients in whom polycythemia and chronic hypertension are associated, the so-called polycythemia hypertonica of Geisböck.²⁹ These cases differ from ordinary polycythemia in the absence of an enlarged spleen. That increased viscosity in itself cannot explain hypertension is clear, however,

²⁷ Ueber Ursache und Bedeutung der Herzaffektion Nierenkranker, Samml. klin. Vorträge, 1906, No. 408 (Serio xiv, 18), Inn. Med., No. 123, p. 525.

²⁸ C. Hirsch and Carl Beck, Studien zur Lehre von der Viscosität (inneren Reibung) des lebenden menschlichen Blutes, Deutsch. Arch. f. klin. Med., 1902, lxxii, 560.

²⁹ Die praktische Bedeutung der Blutdruckmessung, Verhandl. d. Kong. f. inn. Med., 1904, xxi, 97. Die Bedeutung der Blutdruckmessung f. die Praxis, Deutsch. Arch. f. klin. Med., 1905, lxxxiii, 363.

from such an example as that reported by Lommel.³⁰ In his patient, extreme polycythemia was unassociated with rise in blood pressure during life or hypertrophy of the heart at autopsy. Lucas³¹ has recently reviewed 189 cases of erythremia and finds that hypertension existed in only a third.

Changes in the right heart are most often lacking in young persons dying accidentally or without a long illness. I have seen exquisite concentric hypertrophy of the left ventricle alone in a girl of sixteen, with extremely contracted kidneys, who died in uremic convulsions. The weighings of Hirsch³² by Müller's method have shown that the usual sequence of events is (1) hypertrophy of the left ventricle, (2) later in the disease the development of disturbances of compensation, (3) then consecutive hypertrophy of the right ventricle. That another factor may perhaps be involved is suggested by Stewart's³³ study of cardiac hypertrophy resulting from the artificial production of aortic insufficiency in dogs, a purely mechanical lesion. All the chambers of the heart in his animals showed some increase in weight, though the increase was by far the greatest for the left ventricle.

In 1908-1909, with the assistance of Carrel, I attempted to study more in detail the increase in blood pressure following reduction of kidney substance.³⁴ As it is not possible to take innumerable blood-pressure readings directly from an artery, I devised a modified Riva-Rocci method,³⁵ by means of which I was enabled to take approximate readings from the foreleg of the dog. The blood pressure was studied in twenty-three dogs. On ten an operation for the excision of one kidney was made, with infarction of a considerable portion of the remaining kidney by ligation of branches of the renal artery at the hilum. Some of the animals were lost because of too extreme reduction of kidney substance and from accidental causes. One dog (No. 19) survived the operation thirty-nine days; he did well for twenty-one days, but then went into a state of progressive cachexia, with gastro-intestinal disturbances, as described by Bradford³⁶ and by Pearce.³⁷ The blood pressure

³⁰ Ueber Polyerythraemia mit Milztumor, *Deutsch. Arch. f. klin. Med.*, 1906, lxxvii, 338.

³¹ Erythremia or Polyerythemia, with Chronic Cyanosis and Splenomegaly, *Arch. Int. Med.*, 1912, x, 597.

³² Ueber die Beziehungen zwischen dem Herzmuskel und die Körpermuskulatur, und über sein Verhalten bei Herzhypertrophien, *Deutsch. Arch. f. klin. Med.*, 1899, lxiv, 597.

³³ An Experimental Contribution to the Study of Cardiac Hypertrophy, *Jour. Exp. Med.*, 1911, xiii, 187.

³⁴ Theodore C. Janeway, Note on the Blood-pressure Changes Following Reduction of the Renal Arterial Circulation, *Proc. Soc. Exp. Biol. and Med.*, 1909, vi, 109 to 111.

³⁵ Theodore C. Janeway, A Modification of the Riva-Rocci Method of Determining Blood-Pressure for Use on the Dog, *Proc. Soc. Exp. Biol. and Med.*, 1909, vi, 108.

³⁶ The Results following Partial Nephrectomy and the Influence of the Kidney upon Metabolism, *Jour. Phys.*, 1899, xxiii, 415.

³⁷ The Influence of the Reduction of Kidney Substance upon Nitrogenous Metabolism, *Jour. Exp. Med.*, 1908, x, 632. A Study of Experimental Reduction of Kidney Tissue, with Special Reference to the Changes in that Remaining, *Jour. Exp. Med.*, 1908, x, 745.

which had averaged 106 mm. before operation and 127 mm. during the first twenty-one days, fell to an average of 83 during the terminal illness.

BLOOD-PRESSURE READINGS IN MILLIMETERS ON DOG NO. 19.

	Maximum.	Minimum.	Average.
Before operation, 15 days, 4 readings . . .	110	100	106
After operation, 21 days, 7 readings . . .	135	120	127
Terminal period, 14 days, 3 readings . . .	110	70	83

The above is analogous to what one sees occasionally when human beings with high pressure develop a terminal infection or wasting disease. Two dogs showed unequivocal, sustained hypertension; they were followed for 104 and 163 days respectively. Polyuria was evident, as in former experiments of this type. Albumin was usually present in the urine, which Pearce³⁸ has suggested evidenced nephritis in the remaining functioning kidney; but except in the neighborhood of the infarct the histologic appearances were normal.

BLOOD-PRESSURE READINGS IN MILLIMETERS ON DOG NO. 12.

	Maximum.	Minimum.	Average.
Before operation, 45 days, 7 readings	110	80	90
After operation, first 28 days, 8 readings	120	100	111
After operation, second 28 days, 10 readings	140	110	119
After operation, third 28 days, 11 readings	150	110	121
After operation, fourth 28 days, 12 readings	140	110	126
After operation, fifth 28 days, 7 readings	130	115	120
After operation, final 23 days, 7 readings	145	120	134

BLOOD-PRESSURE READINGS IN MILLIMETERS ON DOG NO. 20.

	Maximum.	Minimum.	Average.
Before operation, 23 days, 11 readings	135	95	117
After operation, first 28 days, 13 readings	175	130	157
After operation, second 28 days, 15 readings	165	130	150
After operation, third 28 days, 6 readings	185	150	158
After operation, fourth 20 days, 6 readings	165	150	156

These experiments, it seems to me, confirm and extend the results obtained by Pässler and Heineke.³⁹ They have not the same validity as a demonstration of the effect of purely quantitative reduction of kidney substance, as the infarcted portion of kidney was left *in situ*. It might be argued that the high blood pressure was the result of absorption of the products of disintegration of kidney tissue in the infarcted area, but the duration of the high blood pressure for weeks after the infarct was converted into a mass of partly calcified fibrous tissue would seem to make this criticism negligible.

³⁸ The Problem of Experimental Nephritis, Harvey Lectures, Philadelphia, 1909-10, p. 55.

³⁹ Versuche zur Pathologie des Morbus Brightii, Verhandl. d. deutsch. path. Gesellsch., 1905, x, 99.

From the standpoint of the dog, therefore, it seems clear, as Pässler and Heineke have shown, that moderate hypertension follows the quantitative reduction of kidney tissue to about a third of the total. My experiments show that such hypertension may be maintained for a long period. The rise in blood pressure thus produced is therefore more analogous to the hypertension of chronic nephritis in man than the transient hypertension of most animal experiments dealing with this problem. By what mechanism this increased blood pressure is brought about is wholly obscure, but that it must be associated, as Pässler⁴⁰ predicates, with increased tonus of the systemic arteries seems inescapable.

RENIN. Many attempts have been made to discover chemical substances exerting a pressor effect which could be conceived as accumulating in the blood in kidney disease. Simple retention of urea or other metabolites failed to accord with the facts. In 1898 Tigerstedt and Bergman⁴¹ extracted from the rabbit's kidney a substance which they called renin and which, when injected into animals produced a rise of blood pressure. H. Batty Shaw⁴² reviewed this subject extensively in the Goulstonian lectures for 1906, and advocated with enthusiasm the theory of autolysis of the kidney, with liberation of some pressor substance of this type, as the explanation of nephritic hypertension. Bingel and Strauss⁴³ have confirmed the pressor effects of renin. More recently, Pearce⁴⁴ has investigated the effects of kidney extracts from various animals on the same and other animal species, with altogether variable results. For instance the extract of dog kidney injected into the dog caused a decided fall in blood pressure; the same was true of rabbit's extract; while rabbit kidney and dog kidney extracts injected into the rabbit produced a slight rise. J. L. and E. M. Miller⁴⁵ have failed to obtain pressor effects from saline extracts of kidney or of any other organ except the spleen, hypophysis, and adrenal. It is, moreover, an acknowledged clinical fact that hypertension is most extreme in those exquisitely chronic types of nephritis in which the breaking down of kidney substance must be at a minimum if there is any at all. This fact, to my mind, so argues against the hypotheses that have been cited that I think it is reasonable to dismiss them from consideration.

EPINEPHRIN. The search for a chemical principle within the body by which to explain the phenomenon of increased blood

⁴⁰ Ueber Ursache und Bedeutung der Herzaffektion Nierenkranker, Samml. klin. Vorträge, 1906, No. 408 (Serie xiv, 18), Inn. Med., No. 123, p. 525.

⁴¹ Niere und Kreislauf, Skand. Arch. f. Physiol., 1898, viii, 223.

⁴² Auto-intoxication: its Relation to Certain Disturbance of Blood Pressure, 1906, Lancet, i, 1295, 1375, 1455.

⁴³ Ueber die blutdrucksteigernde Substanz der Niere, Deutsch. Arch. f. klin. Med., 1909, xevi, 476.

⁴⁴ An Experimental Study of the Influence of Kidney Extracts and of the Serum of Animals with Renal Lesions upon the Blood Pressure, Jour. Exp. Med., 1909, xi, 430.

⁴⁵ The Effect on Blood Pressure of Organ Extracts, Jour. Phys., 1911, xliii, 242.

pressure seemed to have attained its goal in Oliver and Schäfer's⁴⁶ discovery of the remarkable effects produced by extracts of the suprarenal gland. The development of the adrenalinemia theory of hypertension makes a fascinating chapter in the history of speculative medicine. It is so rich in lessons and belief in the theory is so widespread that I propose to sketch it in detail. The hypothesis that increased secretion of the suprarenals might be the long-sought cause of nephritic hypertension was first proposed by Neusser,⁴⁷ but merely as a shrewd guess, from a single clinical case of chronic Bright's disease with carcinoma of one adrenal. The first attempts to bring forward arguments in support of the assumption were made in France. Vaquez⁴⁸ in 1904, in a paper read before the French Congress of Medicine, produced some autopsy observations made by his pupils, Aubertin and Ambard, showing the presence of nodular hyperplasia of the suprarenals, and of actual adenomas in cases of hypertensive nephritis, and brought into line with them Josue's recent studies of the arterial lesions produced by epinephrin. This evidence was received with enthusiasm; but further anatomic investigations, particularly those of Landau,⁴⁹ Pearce,⁵⁰ Thomas,⁵¹ and Borberg,⁵² made on extensive material, have failed to show a constant relation between anatomic lesions of the adrenals and the hypertension of nephritis or arteriosclerosis. Similar suprarenal lesions have also been found in persons dying of other diseases. To a large extent it now seems probable that the changes found in the gland are the result of local arteriosclerosis of its own vessels rather than *vice versa*. The experimental lesions produced by epinephrin, moreover, are quite unlike human arteriosclerosis. Pearce⁵³ suggests that hyperplasia of the adrenal probably represents the effect of some factor operating in the later period of life, during which chronic nephritis and arterial affections are most frequent. The relations are evidently complicated and the anatomic evidence of excessive suprarenal function is unconvincing. Perhaps the most extensive work upon the subject is Ingier and Schmorl's⁵⁴ determination of the epinephrin content of the adrenals in 517 autopsies. They found an

⁴⁶ The Physiological Effects of Extracts of the Suprarenal Capsules, Jour. Phys., 1895, xviii, 231.

⁴⁷ Artur Biedl, Innere Sekretion, Berlin, 1910, p. 243.

⁴⁸ Hypertension, Proc. Congrès Français de Méd., 1904, p. 338.

⁴⁹ Ueber die anatomischen Veränderungen in den Nebennieren bei Arteriosklerose, Zeitschr. f. klin. Med., 1907, lxiv, 227.

⁵⁰ The Relation of Lesions of the Adrenal Gland to Chronic Nephritis and to Arteriosclerosis: an Anatomical Study, Jour. Exp. Med., 1908, x, 735.

⁵¹ Ueber Veränderungen der Nebennieren, insbesondere bei Schrumpfnieren, Beiträge z. path. Anat. u. z. allgem. Path., 1910, xlix, 228.

⁵² Das chromaffine Gewebe. Nebennierenuntersuchungen, Skand. Arch. f. Physiol., 1912, xxviii, 91 (abstract, Zentralbl. f. d. gesamm. inn. Med., 1913, iv, 383).

⁵³ The Relation of Lesions of the Adrenal Gland to Chronic Nephritis and to Arteriosclerosis: an Anatomical Study, Jour. Exp. Med., 1908, x, 735.

⁵⁴ Ueber den Adrenalingehalt der Nebennieren, Deutsch. Arch. f. klin. Med., 1911, civ, 262.

increase of epinephrin in the glands in acute nephritis, and in seventeen patients with chronic nephritis, with higher values on the average in those having high blood pressure and hypertrophied hearts. On the other hand their highest figure, almost three times the normal average, was from an individual without either an hypertrophied heart or arteriosclerosis; and the three next highest figures were from similar cases. Again, the subject with the greatest cardiac hypertrophy showed a far lower epinephrin content, actually less than the normal. These results can be more readily explained along the lines suggested by Pearce.⁵⁵

The well-marked hypotension of Addison's disease and the rapid death with a sharp fall in blood pressure which followed the earlier extirpations of the adrenals were assumed to be the reverse side of the picture. To many minds the evidence of diminished adrenal secretion seemed so clear that the assumption of increased adrenal secretion as the cause of the opposite effect upon blood pressure and heart was an easy step. But the more the cause of death after removal of the adrenals has been studied and the better the operative technique employed, the further have the effects upon blood pressure receded into the background. Many investigators have now succeeded in extirpating the adrenals, or in excluding them from the circulation by ligature of their veins, without producing immediate effects upon blood pressure. After Hultgren and Andersson's⁵⁶ technically perfect removal of the adrenals the blood pressure in some of the animals remained normal for two or three days. In this country Hoskins and McClure⁵⁷ have recently performed similar experiments. They seem to me of crucial importance. The effect of epinephrin is so transient that, were the normal tonus of the bloodvessels dependent upon its presence, the exclusion of the suprarenals from the circulation must cause a prompt and unmistakable fall in blood pressure. Furthermore, there seems reason to believe that the cortex, not the medulla of the adrenal, is the structure essential to life. The cortex, as is well known, plays no part in the elaboration of epinephrin. The whole question is extensively discussed by Biedl⁵⁸ and by Bayer;⁵⁹ Biedl seems to lean toward this view. Plainly therefore the hypotension of Addison's disease can in nowise be used as an argument to bolster up the assumption that hypertension is an affair of hypersecretion of the adrenals.

With the increasing activity of physiologists in investigating the action of epinephrin, methods became available for its identifi-

⁵⁵ *The Relation of Lesions of the Adrenal Gland to Chronic Nephritis and to Arteriosclerosis: an Anatomical Study*, Jour. Exp. Med., 1908, x, 735.

⁵⁶ Artur Biedl, *Innere Sekretion*, Berlin, 1913, 2d edition, p. 373.

⁵⁷ *The Relation of the Adrenal Glands to Blood Pressure*, Amer. Jour. Phys., 1912, xxx, 192.

⁵⁸ *Innere Sekretion*, Berlin, 1913, 2d edition.

⁵⁹ *Normale und pathologische Physiologie des chromaffinen Gewebes der Nebennieren*, Ergebn. d. allg. Path. u. pathol. Anat., 1910, xiv, 11, 1.

cation in exceedingly dilute solutions. Batelli⁶⁰ reported in 1902 that he obtained a pressor effect by injecting concentrated dog serum into rabbits which corresponded to an epinephrin concentration in the blood of 1 to 20,000,000. The first clinical work to attract widespread attention to the supposed presence of epinephrin in the circulating blood of nephritics was a publication by Schur and Wiesel.⁶¹ Their test object was the excised eye of the frog, which dilates with epinephrin, a method first described by Meltzer.⁶² They also claimed to identify epinephrin chemically by the ferric chloride reaction. Schur and Wiesel⁶³ prophesied that it would soon be proved that the high blood pressure, the cardiac hypertrophy, and the vascular changes of kidney disease are related to increased activity of the chromaffin system, which was at that time beginning to attract wide notice. Schlager⁶⁴ promptly made tests by the Meyer artery strip method, using normal sera, and in ten experiments, nephritic sera from hypertensive patients. He found that normal serum, even after removal of the albumin, always contained a constrictor substance which resisted dialysis, was diminished by concentration *in vacuo*, and therefore resembled epinephrin. The nephritic sera in all but one case produced much less constriction than normal sera. He concluded therefore that Schur and Wiesel's results had no validity because they had been unable to identify an epinephrin-like substance in normal blood, and held that the hypothesis of a connection between nephritic hypertension and adrenal function was as yet unproved. Schlager⁶⁵ made a number of other studies by the Meyer⁶⁶ method, and came to the conclusion that arteries would not react to epinephrin in any but homologous blood. Fraenkel⁶⁷ using the uterus suspension as a test object; Trendelenburg⁶⁸ using the frog perfusion preparation of Læwen,⁶⁹ and later Bröking and Trendelenburg,⁷⁰

⁶⁰ Présence d'adrénaline dans le sang d'animaux. Son dosage, Comptes rendus de la Soc. de Biol., 1902, liv, 1179.

⁶¹ Ueber eine der Adrenalinwirkung analoge Wirkung des Blutserums von Nephritikern auf das Froschauge, Wien. klin. Woch., 1907, xx, 699.

⁶² The Effect of Suprarenal Extract upon the Pupils of Frogs, Amer. Jour. Phys., 1904, xi, 449.

⁶³ Zur Frage drucksteigernder Substanzen im Blute bei chronischer Nephritis, Deutsch. med. Woch., 1907, xxxiii, 2136.

⁶⁴ Zur Frage drucksteigernder Substanzen im Blute bei chronischer Nephritis, Deutsch. med. Woch., 1907, xxxiii, 1897.

⁶⁵ Zur Frage der blutdrucksteigernden Substanzen im Blute bei Nephritis, Münch. med. Woch., 1908, lv, 2604.

⁶⁶ Ueber einige Eigenschaften der Gefässmuskulatur, mit besonderer Berücksichtigung der Adrenalinwirkung, Zeitschr. f. Biol., 1906, xxx, 352.

⁶⁷ Ueber den Gehalt des Blutes an Adrenalin bei chronischer Nephritis und Morbus Basedowii, Arch. f. exper. Path. u. Pharmacol., 1909, lx, 395.

⁶⁸ Bestimmung des Adrenalingehaltes im normalen Blut, sowie beim Abklingen der Wirkung einer einmaligen intravenösen Adrenalininjektion mittels physiologischer Messmethode, Arch. f. exper. Path. u. Pharmacol., 1910, lxiii, 161.

⁶⁹ Quantitative Untersuchungen über die Gefässwirkung von Suprarenin, Arch. f. exper. Path. u. Pharmacol., 1904, li, 415.

⁷⁰ Adrenalin-nachweis und Adrenalingehalt des menschlichen Blutes, Deutsch. Arch. f. klin. Med., 1911, ciii, 168.

all failed to get greater constrictor effects from the blood of patients having high pressure than with blood from normal persons. Kretschmer's⁷¹ results with the Meyer method were positive in acute and negative in chronic nephritis. However, the extreme vasoconstriction produced by the defibrinated blood or serum which all used seemed to reproduce the effect of epinephrin so exactly that the presence of this in normal blood was accepted without question.

On the basis of Langley's and Elliott's studies of the relation of epinephrin to the sympathetic nervous system⁷² it began to be assumed that the maintenance of normal vascular tonus in the intact animal and man must be altogether dependent upon the constant secretion of epinephrin into the blood by the chromaffin tissue in the medulla of the suprarenal and elsewhere. The more this was taken for granted, however, the more difficult did it become to understand why an epinephrin effect was so often absent in states of high blood pressure. In October, 1911, G. N. Stewart⁷³ published a severe criticism of all these experiments as based upon inadequate evidence that epinephrin was the substance causing the reactions described. He called attention to the fact, which most of the clinical investigators had disregarded, that the property of stimulating the smooth muscle of artery or pregnant uterus is not peculiar to epinephrin. He suggested that as epinephrin evokes from certain other smooth muscle preparations, the intestinal ring for instance, the opposite effect, inhibition with loss of tone, no test for it in complex body fluids should be considered positive which did not demonstrate both types of reaction in the sample examined.

The beautiful dream of adrenalinemia, however, was not seriously disturbed until O'Connor,⁷⁴ in March, 1912, published the results of his painstaking and ingenious investigation of the subject. He proved clearly that the vasoconstrictor substance in defibrinated blood and serum, which had been mistaken for epinephrin, was equally stimulating to intestinal peristalsis, and was therefore from this standpoint the antagonist of epinephrin. He furthermore proved that no constrictor effect was produced by blood which was prevented from coagulating by the addition of citrate or hirudin. The supposed epinephrin of defibrinated blood serum was apparently some substance produced during the process of clotting and not present in the circulating blood at all. Definite evidence of epinephrin in the blood he could obtain only in that from the adrenal veins.

⁷¹ Ueber die Actiologie der nephritischen Blutdrucksteigerung und vergleichende experimentelle Untersuchungen über blutdrucksteigernde Substanzen, Kong. f. inn. Med., 1910, xxvii, 731.

⁷² Artur Biedl, Innere Sekretion, Berlin, 1910, p. 212.

⁷³ So-called Biological Tests for Adrenalin in Blood, with Some Observations on Arterial Hypertonus, Jour. Exper. Med., 1911, xiv, 377.

⁷⁴ Ueber den Adrenalingehalt des Blutes, Arch. f. exper. Path. u. Pharmacol., 1912, lxvii, 195.

The further researches of Stewart,⁷⁵ published very recently, while confirming the absence of epinephrin reactions in peripheral blood, go to show that the whole subject is complicated and that the mere prevention of clotting does not always suffice to make shed blood an indifferent fluid to smooth muscle. Bloods kept from clotting by citrate, hirudin, and peptone are not identical in their effects. These studies again emphasize the need for extreme caution in interpreting the biologic reactions obtained with so complex a fluid as blood as due to any one supposed constituent.

Before the publication of O'Connor's article, Park and the writer,⁷⁶ as the result of a long series of experiments made by a modified Meyer method, had already reached the conclusion that the vasoconstrictor substance of defibrinated blood was not epinephrin. We used as our test objects rings of the carotid artery of the ox which are constricted by epinephrin, and rings of the coronary which undergo dilatation.⁷⁷ Defibrinated blood and serum produced extreme constriction of both preparations. The character of the curve was different from that produced by epinephrin; it was similar to that of barium chloride, a substance known to act directly upon smooth muscle, whereas the point of attack of epinephrin is the so-called "receptive" substance, the neuromuscular junction between the sympathetic nerve fiber and the smooth muscle. It was clear that the serum constrictor substance acted upon smooth muscle directly and had no relation to its sympathetic innervation. We had made a number of unsuccessful attempts to identify low dilutions of epinephrin in serum. After the publication of O'Connor's work we studied normal human blood and blood from six patients having high pressure, with and without nephritis. In most of the experiments we prevented clotting of the blood by the use of hirudin, in a few by citrate. Neither in normal blood nor in the blood from hypertensive patients could any definite trace of an epinephrin effect be obtained.

O'Connor's results have also been amply confirmed by Schultz⁷⁸ who has, however, made no studies of nephritic blood. Using trustworthy methods, Cannon⁷⁹ and his collaborators, and Hoskins and McClure⁸⁰ have identified epinephrin in blood from the adrenal veins. Stewart⁸¹ has only succeeded when the gland was disturbed or stimulated. He has failed to obtain any evidence of its existence in pathological sera.

⁷⁵ A Comparison of the Action of Plasma and Serum on Certain Objects Used in Biologic Tests for Epinephrin, *Jour. Exper. Med.*, 1913, xvii, 152.

⁷⁶ Theodore C. Janeway and Edwards A. Park, The Question of Epinephrin in the Circulation and its Relation to Blood Pressure, *Jour. Exper. Med.*, 1912, xvi, 541.

⁷⁷ Edwards A. Park, Observation with Regard to the Action of Epinephrin on the Coronary Artery, *Jour. Exper. Med.*, 1912, xvi, 532.

⁷⁸ Physiological Studies in Anaphylaxis, *Bull. Hyg. Lab., United States Public Health and Marine Hospital Service*, 1912, No. 80.

⁷⁹ Emotional Stimulation of Adrenal Secretion, *Amer. Jour. Physiol.*, 1911, xxviii, 64.

⁸⁰ The Adrenal Glands and Blood Pressure, *Arch. Int. Med.*, 1912, x, 343.

Hoskins and McClure⁸² feel confident that they have shown that the quantity of epinephrin necessary to produce a minimal rise in blood pressure is from ten to twenty times the amount secreted by the suprarenal glands per minute. As they have further shown that the injection of an amount sufficient to raise blood pressure causes a complete inhibition of intestinal peristalsis, they argue that adrenal secretion cannot be a direct factor in the maintenance of the normal tonus of the vasomotor system. They agree with O'Connor⁸³ in estimating the probable epinephrin concentration of general arterial and venous blood at 1 in 200,000,000, an amount undetectable by the most delicate methods.

The possible assumption remained that repeated doses of epinephrin below the minimum effective single dose might increase the tone of the vessels. Park has recently tested this for me on the artery strip. His results have been absolutely negative. Lieb has also performed a few experiments to try on the isolated vessel the supposed synergism of hypophysis extract and epinephrin, which Kepinow⁸⁴ claimed to find. He has been unable to confirm it.

The work of Cannon⁸⁵ and his collaborators, already alluded to, showed a marked increase in epinephrin output under the influence of anger, fear, and strong sensory stimulation. The splanchnic nerve seems to contain secretory fibers for the adrenal. Two articles by von Anrep⁸⁶ (from Starling's laboratory), which have just appeared, show that the normal effect of splanchnic stimulation in an intact animal is a short, primary rise in blood pressure, followed by a secondary rise, which is accompanied by increased tonus of the heart and marked peripheral vasoconstriction. Similar stimulation, after exclusion of the suprarenals by clamping the vein, results only in a moderate rise in pressure, continuous with the primary rise, with dilatation—not constriction—of the heart and the peripheral arteries. The conclusion drawn seems warranted—that the secondary effects of splanchnic stimulation are dependent upon the discharge of epinephrin into the blood stream.

BLOOD SUGAR. The problem has been approached from one other side—namely, by the investigation of the blood sugar. It is well known that the injection of epinephrin into an animal whose liver contains glycogen, results in an increase of sugar in the blood, which if it reaches a sufficiently high percentage, produces transient glycosuria. It has therefore been reasoned that if hypertension be

⁸² The Alleged Existence of Adrenalin (Epinephrin) in Pathological Sera, *Jour. Exper. Med.*, 1912, xv, 547.

⁸³ The Adrenal Glands and Blood Pressure, *Arch. Int. Med.*, 1912, x, 343.

⁸⁴ Ueber den Adrenalingehalt des Blutes, *Arch. f. exper. Pnath. u. Pharmakol.*, 1912, lxxvii, 193.

⁸⁵ Ueber den Synergismus von Hypophysisextrakt und Adrenalin, *Arch. f. exper. Path. u. Pharmakol.*, 1912, lxxvii, 247.

⁸⁶ Emotional Stimulation of Adrenal Secretion, *Amer. Jour. Physiol.*, 1911, xxviii, 64.

⁸⁷ On the Part Played by the Suprarenal in the Normal Vascular Reactions of the Body, *Jour. Physiol.*, 1912, xlv, 307. On Local Vascular Reactions and Their Interpretation, *Jour. Physiol.*, 1912, xlv, 318.

associated with increased circulating epinephrin, hyperglycemia should be found. Patients with high blood pressure, with and without nephritis, have therefore been investigated by various observers, with conflicting results.⁸⁷ At present the problem is being investigated in my service at the Presbyterian Hospital by Geyelin. The following table illustrates the most striking hyperglycemia yet observed in chronic nephritis:

HYPERGLYCEMIA IN CHRONIC NEPHRITIS.

Date.	Diet.	Blood sugar per cent.	Urea per cent.	Blood pressure.
Nov. 25	Soft, NaCl poor	0.099	0.168	234 mm.
Dec. 20	Soft, NaCl poor	0.133	0.188	220 mm.
Jan. 18*	Glucose 100 grams. Two hours after glucose ex- creted in urine, 0.26 gram	0.201	..	230 mm.
Jan. 22*	Glucose, 100 grams. Two hours after glucose ex- creted in urine, 0.12 gram	0.192	..	225 mm.
Feb. 8*	N. poor, thirty-six hours after uremic convulsion .	0.1605	0.375	205 mm.

* Epinephrin tests made on samples taken on these days.

It will be noticed that the blood sugar has increased from a figure at the upper limit of normal to a marked hyperglycemia in eleven weeks, while the blood pressure was highest at the first and lowest at the last observation. This increase, while unrelated to the height of the blood pressure, has, however, been coincident with the advance of the kidney lesion, increasing uremic symptoms, and a rise in the urea content of the blood, indicating coincident nitrogen retention. These figures seem to me much more in accord with the theory of renal retention than of epinephrin hyperglycemia, though one cannot interpret them with any positiveness. In view of the possibility of technical errors and of retention of sugar by the diseased kidney, it is the part of wisdom to reserve opinion upon the whole question until extensive work has been done by the newer, accurate methods. Even should hyperglycemia prove to be frequent in such patients, it would be absurd to consider it more than suggestive of increased circulating epinephrin, as it might be dependent upon other wholly unrelated disturbances or renal impermeability.

⁸⁷ Neubauer (Ueber Hyperglykämie bei Hochdrucknephritis und die Beziehungen zwischen Glykämie und Glucosurie beim Diabetes mellitus, *Biochem. Zeitschr.*, 1910, xxv, 284; Nephritis und Blutzucker, *Arch. f. exper. Path. u. Pharmacol.*, 1912, lxvii, 192 to 193), especially, claims to have found marked increases in blood sugar; Hagelberg (*Hypertension und Blutzucker*, Berlin. klin. Woch., 1912, xl, 1877), Wieland (*Oekonomie des Blutzuckers*, *Zentralbl. f. d. gesamm. Physiol. u. Path. d. Stoffwechs.*, 1910, v, 481), and Port (*Hypertension und Blutzucker*, *Deutsch. med. Woch.*, 1913, xxxix, 69) found significant increases only in cases with marked uremic symptoms, eclampsia, or apoplexy; Stilling (*Nephritis und Blutzucker*, *Arch. f. exper. Path. u. Pharmacol.*, 1911, lxvi, 238), Tachau (*Eine neue Methode der Bestimmung des Blutzuckergehaltes*, *Deutsch. Arch. f. klin. Med.*, 1911, cii, 597), Schirokauer (*Zur Methodik der Blutzuckerbestimmung*, Berlin. klin. Woch., 1912, xxxviii, 1783), and Frank (*Bestehen Beziehungen zwischen chromaffinem System und der chronischen Hypertonie des Menschen*, *Deutsch. Arch. f. klin. Med.*, 1911, ciii, 397) have failed to find definite hyperglycemia. The latter worked especially with so-called essential hypertension cases.

In addition to this investigation, Lieb and I have recently made one more attempt to identify epinephrin in the peripheral blood from a patient in whom positive results might certainly be expected, if the epinephrin theory of hypertension has any basis. The patient was the one in whom the notable hyperglycemia was found (see page 641). The blood, prevented from clotting by hirudin, was tested on January 18 and 22 and February 8, on the last date thirty-six hours after a uremic convulsion; bleeding was done for therapeutic purposes. On the first date dilatation of the coronary was obtained, but of an extent comparable to that produced by not less than 1 to 10,000,000 epinephrin. At the same time a constriction of the peripheral artery was produced, but the form of the curve was different from any which I have ever seen due to epinephrin. This blood was also tested for its effect in dilating the pupil of the rabbit's eye, after removal of the left superior cervical ganglion. Meltzer⁸⁸ has found this an extraordinarily delicate test for epinephrin. A slight increase in diameter was observed in two such eyes, the control eye and the eyes of control rabbits showing no dilatation, or slight constriction. The light conditions for this test were, however, not entirely satisfactory.

For this reason additional tests were made on January 22. In these the carotid response was typical of epinephrin; the coronary, however, showed a primary constriction, followed after three minutes by a marked dilatation. This cannot be claimed as an epinephrin response, though it is possible that it may be the combination of an epinephrin effect with vasoconstriction from some other substance in the blood. The rabbit intestine test with the same blood was only faintly suggestive, in no way corresponding to the effect which might have been expected from the constriction produced in the carotid. The final test on February 8 gave a satisfactory carotid response, but a constriction of the coronary, followed after a still longer interval than in any other case by dilatation and an inhibition of the intestine so extreme and protracted as to be impossible with any concentration of epinephrin which would not have given the most typical results with the two artery preparations. These findings while in many particulars highly suggestive of the presence of epinephrin, are entirely too variable to permit me to believe that we have identified it.⁸⁹

⁸⁸ Studies on the "Paradoxical" Pupil Dilatation Caused by Adrenalin. I. The Effect of Subcutaneous Injections and Instillations of Adrenalin upon the Pupils of Rabbits, *Amer. Jour. Phys.*, 1904, xi, 28.

⁸⁹ This patient died in uremic coma on February 17. Autopsy revealed an extreme degree of atherosclerotic contracted kidney, and adrenals which weighed 10.37 and 8.71 grams respectively—more than twofold the normal—with abundant medulla. Estimation of the epinephrin in half the left gland, by Folin's new method (Otto Folin, W. B. Cannon, and W. Denis, *A New Calorimetric Method for the Determination of Epinephrin*, *Jour. Biol. Chem.*, 1913, xiii, 477) showed a content of 3.1 milligrams. The determination from the right adrenal was spoiled. The gland was cut so as to divide the medulla as equally as possible. On this basis the total epinephrin content of the two adrenals should have been 13.5 milligrams, three times larger and Schmorl's average figure. Histologic study of the remaining halves of the glands, while showing a large medulla, failed to show a striking increase in chromaffin substance.

In order to test still further the possibility of detecting epinephrin in the blood, Lieb and I have performed a final series of experiments on four dogs. These dogs were anesthetized and samples of blood were drawn from the right femoral artery, one into hirudin and one into citrate solution. Then a continuous infusion of epinephrin in normal saline, according to Kretschmer's method,⁹⁰ was introduced into the right femoral vein. This produced a sudden and extreme hypertension, 200 mm. or over, for at least ten minutes in the shortest experiment. Blood was taken from the left femoral artery at the end of the infusion, while the blood pressure was still high, and its action on carotid and coronary strips and the intestinal segment compared with that of blood drawn before the production of epinephrin hypertension. The results of these four experiments are very disappointing. While in all we obtained positive tests with one or two of the test objects used, in no single experiment did we succeed in producing unequivocal epinephrin reactions in all three test objects. As shown by Stewart,⁹¹ foreign blood has at times very disturbing effects upon these living smooth muscle preparations.

The amount of epinephrin injected into three dogs was 0.05 mg., and for one 0.1 mg. per kilo. Figuring the blood volume of the dog at the minimum of 5 per cent., this would make the concentration of epinephrin, if the blood and epinephrin had been mixed outside the body, 1 in 1,000,000. In our last experiment the intestinal segment showed a mere suggestion of a response, whereas a perfectly distinct effect was produced by blood containing added epinephrin in concentration of 1 to 25,000,000. Such an experiment shows the extreme rapidity of disappearance of epinephrin from the circulation. The immediate fall of pressure at the end of the infusion also suggests prompt destruction or fixation of the substance, though explicable as well by Straub's⁹² theory of toxic action, as illustrated by muscarin.

From these experiments I am persuaded that the attempt, by our present methods, to obtain evidences of epinephrin in the peripheral circulation is fruitless. I should go farther than Stewart⁹³ and insist that no demonstration be considered conclusive which did not show qualitatively typical and quantitatively possible epinephrin effects, simultaneously in three different test objects, inasmuch as many confusingly similar effects may be produced by substances contained in that highly complex fluid, blood. To

⁹⁰ Dauernde Blutdrucksteigerung durch Adrenalin und über den Wirkungsmechanismus des Adrenalins, *Arch. f. exper. Path. u. Pharmacol.*, 1907, lvii, 423.

⁹¹ A Comparison of the Action of Plasma and Serum on Certain Objects Used in Biologic Tests for Epinephrin, *Jour. Exper. Med.*, 1913, xvii, 152.

⁹² Zur chemischen Kinetik der Muskarinwirkung und des Antagonismus Muskarin-Atropin, *Pflüger's Arch.*, 1907, exix, 127.

⁹³ So-called Biologic Tests for Adrenalin in Blood, with Some Observations on Arterial Hypertonus, *Jour. Exper. Med.*, 1911, xiv, 377.

obtain these three reactions, as we have shown, even when epinephrin is known to be the cause of the very high blood pressure, is a matter of great technical difficulty with the biologic test objects at present employed.

To recapitulate, the net result of all this labor is the solid, well-grounded fact that the suprarenal glands, or at least their medullary portions, manufacture a substance, epinephrin, which introduced into the circulating blood produces a rise in the systemic arterial pressure unparalleled in intensity by any other known substance. This rise is extremely transient; but the continuous, steady introduction of epinephrin is capable of maintaining a state of hyper-tonus as long as the introduction is continued. Accompanying this rise in blood pressure is a reduction in volume of the extremities and of many organs, due to local vasoconstriction, so that the actual blood flow through them is diminished. The coronary artery, however, is dilated by epinephrin, and intestinal peristalsis is inhibited and intestinal tonus abolished. The bronchi in a state of spasm are also relaxed by epinephrin. It is probable that during life epinephrin is constantly finding its way from the adrenals into the general circulation, but except in the blood of the adrenal veins, epinephrin has never been positively identified in the general circulation of the normal animal or man. From all the quantitative studies that have been made, as well as from other considerations, it cannot at present be assumed that epinephrin exists in the general circulation in sufficient concentration to manifest any of its physiologic actions; but during stimulation of the splanchnic nerve, either directly, reflexly, or psychically, the rate of epinephrin discharge into the circulation may be markedly increased and its action become evident. This, as Hoskins and McClure⁹⁴ suggest, should probably be regarded as a reserve mechanism of the organism to meet emergencies. Up to the present time epinephrin has not been proved to play any part in the maintenance of normal vascular tonus. There is no convincing evidence, anatomic or physiologic, for any theory connecting the adrenal glands or increased circulating epinephrin with states of high blood pressure, with or without nephritis. That for some types of hypertension, or for certain acute and transient crises of hypertension, increased epinephrin discharge may in the future be demonstrated as the cause can be neither affirmed nor denied.

II. CLINICAL FACTS. From the contentious realm of theory and experiment I ask you to return to the more peaceful, though perhaps prosaic, domain of clinical facts. Experimental medicine has not as yet solved the riddle of hypertension; there is need for further work in that field. Nor can clinical medicine make this claim; but the facts gained by the observation of human blood pressure

⁹⁴ The Adrenal Glands and Blood Pressure, *Arch. Int. Med.*, 1912, x, 343.

in disease have added greatly to our knowledge of the pathology of the circulation. They are fundamental to an adequate understanding of the theoretic problems to be solved in the laboratory and the practical problems to be dealt with at the bedside.

What do we mean by high blood pressure? That question is more easily answered today than it was nine years ago, because the requirement of a blood pressure reading by many life insurance companies as a part of the examination of the applicant has made available the records of large series of normal individuals. From the compilations of Woley,⁹⁵ Fisher,⁹⁶ and Cook⁹⁷ it is clear, as I had held previously,⁹⁸ that a constant systolic blood pressure of 160 mm. or over is pathologic. It seems probable, as Cook suggests, that more extended observations will make 150 mm. the upper normal limit. Before middle life pressures of over 135 mm. are suspicious, above 145 mm. abnormal. In Woley's series, the average for women was 7.5 mm. lower. First readings in any person are apt to be higher than subsequent ones. When the use of the sphygmomanometer becomes as much a matter of daily routine as the taking of temperature, a still more accurate guide to pathologic variations in blood pressure will be afforded by comparing the previously recorded normal pressure of the person in question. I cannot too strongly urge on practitioners the need for keeping occasional records of the arterial pressure of all patients in order that early evidences of disease may be recognized and that our knowledge of the manner in which hypertension develops may be extended.

High blood pressure is a symptom so common that its chief manifestations are familiar to all physicians. General impressions, however, may mislead; and in order that I might present a basis of definite facts, I have made an analysis of the histories of 459 private patients whose systolic blood pressure registered over 165 mm. These records extend over a period of ten years. Upon this analysis and the survey of a selected group of hospital patients any opinions that I may express are founded.

From a study of this kind it is clear that the patients naturally fall into certain groups as regards symptoms and clinical course. The largest group is made up of individuals well past middle life. The clinical picture which they present is usually that of some degree of cardiac insufficiency, and their death is a cardiac death. Arteriosclerosis is a commonly associated lesion; anginoid attacks are fairly frequent; about 10 per cent. are elderly diabetics. While

⁹⁵ The Normal Variation of the Systolic Blood Pressure, *Jour. Amer. Med. Assoc.*, 1910, iv, 121.

⁹⁶ The Diagnostic Value of the Use of the Sphygmomanometer in Examinations for Life Insurance. Meeting of Association of Life Insurance Medical Directors, October 4, 1911, New York.

⁹⁷ Blood Pressure in Prognosis, *Medical Record*, 1911, lxxx, 959.

⁹⁸ Theodore C. Janeway, Diagnostic Significance of High Arterial Pressure, *AMER. JOUR. MED. SCI.*, 1906, cxxxi, 772.

the bulk of them at some period show albumin, casts, or other urinary changes, usually interpreted as indicating nephritis, and while at autopsy the majority prove to have either arteriosclerotic atrophy of the kidneys or the so-called "primary contracted kidney," it must be borne in mind that during life many of these individuals fail to show any urinary changes other than those of chronic passive congestion. There are also a number of authenticated autopsy cases on record in which the same clinical picture of permanently high blood pressure has been associated with kidneys found to be normal or with only secondary congestion, due to a failing heart. I have seen such patients, and Krehl⁹⁹ and Schlayer¹⁰⁰ have published records of similar ones. When these individuals consult a physician because of even minor symptoms, the blood pressure is usually found already far above normal, and although some reduction and great symptomatic improvement may occur as the result of hygienic and dietetic measures, I have only a single unequivocal record of a patient in whom the pressure returned to the normal for as long as two years. In the main, the treatment of these patients lies in safeguarding the heart. From the clinical standpoint I speak of them as cases of hypertensive cardiovascular disease.

A closely related group shows predominant cerebral symptoms—headache, vertigo, apoplectic attacks. Polyuria is found more frequently in this group and the evidences of severe functional damage to the kidneys. Far more of them die with uremic symptoms. The discrimination between toxic cerebral symptoms and manifestations of focal vascular lesions, or of general cerebral arteriosclerosis, is so often impossible during life that this clinical group must be considered a compound one. On the one hand it contains the older individuals whose important disease is arteriosclerosis of the brain arteries; on the other, younger persons with the so-called primary contracted kidney. A quite similar clinical picture may occasionally be presented by chronic glomerular nephritis.

Many attempts have been made to correlate the clinical picture, the functional disturbance of the kidney as revealed by the newer tests, and its anatomic lesions found at autopsy. None of these has succeeded, and at present it seems a far cry to the day when such attempts will be successful. Schlayer¹⁰¹ remarks with much reason that when we speak of chronic interstitial nephritis we usually have in mind a definite symptom-complex rather than an anatomic picture, and that much of the misunderstanding between

⁹⁹ Ueber die krankhafte Erhöhung des arteriellen Druckes, *Deutsch. med. Woch.*, 1905, xxxi, 1872.

¹⁰⁰ Untersuchungen über die Funktion kranker Nieren, *Deutsch. Arch. f. klin. Med.*, 1911, cii, 371.

¹⁰¹ Neue klinische Anschauungen über Nephritis, *Beihefte z. med. Klin.*, 1912, viii, 9, 211.

pathologists and clinicians has arisen from this fact. It seems to me that we should recognize clearly that the differentiation of the various anatomic types of nephritis is altogether beyond the powers of clinical diagnosis. Fortunately it is not of great import for us as internists, for we are practically concerned with structural changes only insofar as they give rise to disturbances of function, can be utilized for diagnosis, or afford us data for prognosis. Rarely, indeed, can we influence them directly. The kidney is a highly complex organ and the contribution of each of its structurally differentiated parts to its total function is unknown. If correlation of structure and function is thus still impossible to the physiologist, the physician need not be ashamed of his failure to harmonize them when diseased. For the present, in the clinical study of renal disease, the aim must be to achieve an exact analysis of the perverted functions and to discover the evidently remote causes, as a basis for treatment and prevention. I believe that the conception of hypertensive cardiovascular disease is justified on this physiologic basis.

When so obvious a disturbance of the circulation exists and investigation of the kidney function shows no changes of importance it is immaterial what may be the exact appearance of the kidney; the patient must be treated from the standpoint of the circulatory disorder. The more recent pathologic anatomic studies seem to justify this rather barefaced clinical point of view. In particular the work of Jores,¹⁰² Aschoff,¹⁰³ and Gaskell¹⁰⁴ shows a return of pathologists to the fundamental idea which Gull and Sutton¹⁰⁵ enunciated—namely, that the real disease back of what we call chronic interstitial nephritis is a disease of the small blood-vessels and that the lesions of the kidney are secondary manifestations. Gull and Sutton may have been misled by inadequate histologic methods into an erroneous interpretation of the vascular lesion, but their arteriocapillary fibrosis stood for the conception of primary vascular disease. The return to the interpretation of the primary contracted kidney as essentially a disorder of the kidney arterioles has been facilitated by Löhlein's¹⁰⁶ differentiation of the secondary contracted kidney, which arises out of a true glomerular nephritis, from the former confused group of atrophic kidneys. While there may be an overlapping of types and various combinations of lesions within the same kidney, and while it is

¹⁰² Ueber die Arteriosklerose der kleinen Organarterien und ihre Beziehungen zur Nephritis, *Virehow's Arch.*, 1904, clxxviii, 367.

¹⁰³ Kritisches zur Lehre von der Nephritis und den Nephropathien, *Med. Klinik*, 1913, ix, 18.

¹⁰⁴ On the Changes in Glomeruli and Arteries in Inflammatory and Arteriosclerotic Kidney Disease, *Jour. Path. and Bact.*, 1912, xvi, 287.

¹⁰⁵ On the Pathology of the Morbid State Commonly Called Chronic Bright's Disease with Contracted Kidney, *Med.-Chi. Trans.*, 1872, lv, 273.

¹⁰⁶ Ueber Nephritis nach dem heutigen Stande der pathologisch-anatomischen Forschung, *Ergebn. d. inn. Med. u. Kinderh.*, 1910, v, 411.

still beyond the possibilities to agree upon either the clinical symptoms or the functional disturbances which are associated with these different types—as such studies as those of Volhard¹⁰⁷ and Frey¹⁰⁸ show—there does seem to be sufficient anatomic basis for the belief that the hypertensive cardiovascular disease which we recognize clinically is not primarily nephritic hypertension (in the strict sense of the term) but widespread disease of the arterioles in various internal organs.¹⁰⁹ The disease in its fully developed form involves the kidney, producing the small, red, granular, or primary contracted kidney; but occasionally it leaves the kidney untouched. In its course arteriosclerosis of the larger vessels may develop, hypertrophy of the heart is frequent, and death by apoplexy a common mode. On the other hand arteriosclerosis of the larger vessels may spread peripherally, as it were, and become associated with a similar clinical picture, though less constantly leading to high blood pressure and a hypertrophied heart. This primary arteriosclerotic disease produces the patchy arteriosclerotic atrophy of the kidney rather than the more diffuse changes of the arteriolar disease. Clinically this form is perhaps more commonly associated with an insufficient heart. From the standpoint of physiology the high blood pressure is the evidence of arteriolar disease rather than renal, though it is premature to consider the relation quantitative in any sense. It must be interpreted as a sign of abnormal irritability of the constrictor mechanism. Whether it precedes the development of the anatomic lesions, as Allbutt¹¹⁰ and the English school have held, as Huchard¹¹¹ meant by his term “pre-sclerosis,” as von Basch¹¹² taught in his conception of “angiosclerosis,” and as Jores¹¹³ seems to believe, cannot be regarded as settled. That it is, however, primarily dependent upon processes without the kidney seems altogether probable.

Have we any clue to the origin of this persistent vascular spasm? We have seen that the epinephrin theory is without verification. Were it proved it would only explain the mechanism, not its cause, and carry the problem one step farther back. Many experienced clinicians have believed that high blood pressure is in some way related to overindulgence in food, the abuse of tobacco, of coffee, and other poisons, and the sedentary life, which characterize the well-to-do in our western civilization. Allbutt's hyperpiesis expresses this view. The results of treatment sometimes lend strong support

¹⁰⁷ Ueber die funktionelle Unterscheidung der Schrumpfnieren, Kongr. f. inn. Med., 1910, xxvii, 735.

¹⁰⁸ Zur Pathologie der chronischen Nephritiden, Deutsch. Arch. f. klin. Med., 1912, evi, 347.

¹⁰⁹ Kritisches zur Lehre von der Nephritis und den Nephropathien, Med. Klinik, 1913, ix, 18.

¹¹⁰ Arteriosclerosis and the Kidneys, British Medical Journal, April 15 and 22, 1911 i, 853, 992.

¹¹¹ Traité cliniques des maladies du cœur et des vaisseaux, Paris, 1893.

¹¹² Die Herzkrankheiten bei Arteriosklerose, Berlin, 1901.

¹¹³ Ueber die Beziehungen der Schrumpfnieren zur Herzhypertrophie vom pathologisch-anatomischen Standpunkt, Verhandl. deutsch. path. Gesellsch., 1908, xii, 187 (see editorial, Jour. Amer. Med. Assoc., 1909, lü, 565); Deutsch. Arch. f. klin. Med., 1908, xciv, 1.

to it. In a recent case, for instance, a gentleman of sixty-two years, who showed at the subsequent autopsy an early stage of vascular kidney disease, underwent a Tufnell cure for thoracic aneurysm. The systolic pressure fell from 220 to 125 mm., after a hemorrhage once reached 70 mm., and yet returned to 190 mm. before death. Remarkable drops are seen in hospital patients after rest in bed with salt-poor diet, but the pressure usually rises moderately as soon as activity is resumed. Such reports as that of Hecht¹¹⁴ show how much the tension may be modified during sanatorium treatment, in which muscular training, massage, bland diet, limitation of fluid and of salt, and abstinence from tobacco, spices, and coffee coöperate with freedom from home and business cares to reduce the activity of the constrictor mechanisms. How much of this is central, how much peripheral, and which of the many changes in external conditions and internal relations is preponderant in accomplishing the result is not clear. But, again, some persons of abstemious life develop hypertension, and in most of these, treatment effects no marked or permanent change in the blood pressure.

A conspicuous feature in many of these patients is the variability of the pressure, especially the systolic pressure, within short periods, often from hour to hour (Hensen,¹¹⁵ Israel¹¹⁶). All the causes of slight elevation of pressure in the normal person produce exaggerated effects in them. Vasodilators also, such as the nitrites, usually evoke a prompt though temporary response. Only in rare cases do the vessels cease to react. My experience is in entire accord with Matthew,¹¹⁷ Miller,¹¹⁸ and Wallace and Ringer¹¹⁹ in this respect. Intercurrent acute disease usually produces a marked fall. These facts show clearly, I think, that disturbed vasomotor regulation, not permanent vascular obliteration, is the usual important factor. Volhard¹²⁰ makes the interesting observation that this type of disease is rare in Japan, and future statistics of vegetarian races may help to fix responsibility.

Gout and hypertensive nephritis are usually associated, and the clearing up of the causation of gout will illuminate our problem. One poison, however, which in rare cases produces acute gout, is

¹¹⁴ Ueber die diätetische Beeinflussung pathologischer Blutdrucksteigerungen, *Zeitschr. f. klin. Med.*, 1912, lxxvi, 87.

¹¹⁵ Beiträge zur Physiologie und Pathologie des Blutdrucks, *Deutsch. Arch. f. klin. Med.*, 1900, lxxii, 438.

¹¹⁶ Klinische Beobachtungen über das Symptom der Hypertension, *Samml. klin. Vorträge*, Nos. 449 and 450 (Serie xv, 29-30), *Inn. Med.*, No. 135-136, 1907, p. 853.

¹¹⁷ Vasodilators in High Blood Pressure, *Quart. Jour. Med.*, 1909, ii, 261.

¹¹⁸ Hypertension and the Value of the Various Methods for its Reduction, *Jour. Amer. Med. Assoc.*, 1910, liv, 1666.

¹¹⁹ The Lowering of Blood Pressure by the Nitrite Group, *Jour. Amer. Med. Assoc.*, 1909, liii, 1629 and 1630.

¹²⁰ Ueber die funktionelle Unterscheidung der Schrumpfnieren, *Kongr. f. inn. Med.*, 1910, xxvii, 735.

the single cause of hypertensive cardiovascular disease upon which we can definitely put our fingers. That poison is lead. Vaquez¹²¹ and Pal¹²² have shown that lead colic is as truly a vascular crisis with transient hypertension as it is an intestinal cramp with constipation. As acute lead poisoning is thus a cause of marked acute vascular hypertonus, and chronic lead poisoning is known to be prolific of permanent hypertension, arteriosclerosis, and contracted kidney, one is strongly tempted to believe that the eventual anatomic vascular lesions are the sequel of the persistent vascular overstimulation. The suggestion then arises that other poisons as yet unknown act in a similar manner upon the bloodvessels. To carry the train of thought farther is unprofitable, and such poisons must be isolated and their actions demonstrated before such a theory can be useful. That in most cases of high blood pressure they are not retention products in the ordinary sense is clear, as gross retention does not exist in these patients until late.

The theory of intoxication by substances held back by the damaged kidney cannot be entirely discarded, however. The observation of cases with partial or intermittent ureter obstruction taught Cohnheim¹²³ long ago that hypertrophy of the heart and high arterial pressure might result. I have seen excision of the only functioning kidney lead to a rise in blood pressure four days after to 180 mm.; it fell again toward death. Pässler¹²⁴ and Brasch,¹²⁵ report interesting cases of long-standing anuria, due to bilateral ureter compression by pelvic carcinoma in women, with marked hypertension. One case of Brasch's rose from 115 to 210 mm. after three days of anuria. In these instances neither edema nor true uremia occurs, but acute hypertension is the rule. They seem quite analogous to the results of experimental quantitative reduction of kidney substance. Whether this is due to normal metabolites or abnormal compounds is not clear. Pearce's¹²⁶ interesting observations on the depressor substance of dogs' urine suggest the possibility that a normal balance between pressor and depressor substances in the blood may be maintained by the kidney.

I believe that the rise in blood pressure which may accompany anuria in such toxic necroses of the kidney as are produced by bichloride of mercury, for instance, belongs in the same category.

¹²¹ La tension arterielle dans le saturnisme aigu et chronique, *Sémaine Médicale*, 1904, xxiv, 385.

¹²² *Gefässkrisen*, Leipsic, 1905.

¹²³ *Vorlesungen über allgemeine Pathologie*, Berlin, 1880, ii, 397.

¹²⁴ Beitrag zur Pathologie der Nierenkrankheiten, nach klinischer Beobachtungen bei totaler Harnsperrre, *Deutsch. Arch. f. klin. Med.*, 1906, lxxxvii, 569.

¹²⁵ Ueber die klinischen Erscheinungen bei langandauernder Anurie, *Deutsch. Arch. f. klin. Med.*, 1911, ciii, 488-504.

¹²⁶ Concerning the Depressor Substance of Dog's Urine and its Disappearance in Certain Forms of Experimental Acute Nephritis, *Jour. Exper. Med.*, 1910, xii, 2, 128.

Krehl¹²⁷ says this does not occur, but I have seen the pressure rise from 130 mm. on the first to 168 mm. on the fifth day of bichloride poisoning, remaining about 170 mm. until the ninth day and then fall until death on the thirteenth day. Friedrich Müller¹²⁸ reports a similar finding.

I believe it is also probable, from some conspicuous instances of improvement following prostatectomy, that the effect of long-standing obstruction of the urethra may be the superposition of a blood pressure rise of this type on an already existing hypertension. A few other cases that I have seen possibly fall into this category of quantitative renal insufficiency. I have in mind a patient with a blood pressure of 200, who at autopsy showed complete infarction of one kidney, and only chronic passive congestion of the other. A second patient had a rudimentary kidney on one side, with moderate, diffuse nephritis of the other; he died with explosive uremic symptoms. I have also seen cases of gradual destruction of the kidney by bilateral pyonephrosis, with hypertension and terminal uremia. In the later stages of decompensated valvular disease it is the rule to find the blood pressure above the normal, sometimes considerably so; and the sulphonephthalein test gives evidence of a marked impairment of kidney function. Such patients frequently die with cerebral symptoms, much like those seen in uremia. From the functional as contrasted with the anatomic standpoint it seems that chronic passive congestion may produce serious disturbances in the kidney, and that the hypertension seen in such cases may be dependent upon this factor.

It is well known that patients with congenital cystic kidneys in the end develop the clinical picture of contracted kidney, with hypertrophied heart, high pressure, and low gravity urine. I have seen a striking example of this kind. One is tempted to think of the terminal state as one of quantitative reduction of kidney substance to the danger point, and in so doing to strengthen the argument for a more definite relation between kidney function and hypertension than the consideration of the atherosclerotic group seems to warrant.

The rare cases of amyloid disease must be considered for the moment an insoluble mystery. The kidneys are the seat of the most extensive vascular lesions, with practically every glomerulus infiltrated with the waxy substance. Polyuria may be present early, but in pure cases there is no hypertension, and in many there is actually an extreme, subnormal pressure. I have observed two autopsy cases in which the pressure ran from 65 to 90 mm. for weeks. A satisfactory theory of nephritic hypertension must afford an interpretation of such phenomena. Were I convinced

¹²⁷ *Pathologische Physiologie*, 1912, Leipsic, 35.

¹²⁸ Ch. Thorel, *Pathologie der Kreislauforgane*, *Ergebn. d. allg. Pathol. u. pathol. Anat.*, 1910, xiv, II, 133, quotes Friedrich Müller.

of the universal applicability of the epinephrin theory, I should believe that the extensive infiltration of the adrenals with amyloid, which is the rule when the other viscera are waxy, was a ready-made explanation. One cannot deny that this suggestion has a certain plausibility on its face; I offer it as it has occurred to me, without caring to infer much from it either way, until we have more positive evidence as to the relation of the adrenals to normal vascular tonus. I do not consider that the cachexia of these patients is adequate to account for their low blood pressure, though it may be one factor. From the functional standpoint it is important to note that the type of disturbance manifested by the amyloid kidney is usually that of obstinate edema, with marked salt retention. Now of the types of true chronic glomerulotubular nephritis least often associated with any change in the heart or blood pressure, the dropsical form stands out preëminently, and *vice versa*, hypertension is most extreme in those nephritics who exhibit no edema.¹²⁹ We are as yet too ignorant of the relations of the various excretory functions of the kidney, one to another, to base any theory upon such relations. Widal's¹³⁰ classification of the nephritides into albuminuric, hypertensive hydropigenous, and nitrogen retention types, while suggestive in its broad outlines, does scant justice to the infinite variety of nature. Such studies, however, as he has conducted with regard to functional disturbances in the kidney, and especially such accurate analyses of disturbance in the excretion of individual substances as Schlayer¹³¹ and his coworkers have carried on, point the road toward our goal.

Observations of the blood pressure in true acute nephritis, a condition which even pathologists agree is entitled to its name, are scanty. Many observers have failed to find definite hypertension, but one can never be certain how marked the nephritis was. Certainly a moderate, though very definite, rise in blood pressure has in my experience accompanied severe acute nephritis in the few patients that I have been able to observe carefully. A particularly instructive case showed a rise to 165 mm. during the first week in bed, with a rapid fall as diuresis was established. He recovered completely, and my subsequent observations for almost six years have shown a constant pressure of between 115 and 125 mm. Recently a boy in the hospital who had acute nephritis following severe tonsillitis came in with a pressure of 190. He had slight general edema, and a sulphonephthalein output of 54 per cent. In five days his pressure had fallen to 100, the edema had

¹²⁹ A recent case, however, has shown practically complete absence of sulphonephthalein excretion; so the functional impairment was evidently profound.

¹³⁰ Les grands syndromes du mal de Bright, Jour. med. français, January 15, 1911.

¹³¹ Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med., 1909, xciii, 17; Untersuchungen über die Funktion kranker Nieren beim Menschen, Deutsch. Arch. f. klin. Med., 1910, ci, 333; Untersuchungen über die Funktion kranker Nieren, Chronische vaskuläre Nephritiden, Deutsch. Arch. f. klin. Med., 1911, cii, 311.

disappeared, and the phthalein output had risen to 62 per cent. Rolleston¹³² has recently reported a transient rise in blood pressure in twelve out of thirty-three cases of scarlatinal nephritis, mostly mild; the highest pressure reached was 150. Kurt Weigert¹³³ saw a pressure of 240 mm. in severe post-scarlatinal nephritis fall to 170 mm. before death. One of the most striking observations was that of Buttermann,¹³⁴ who observed a rise of 50 mm. within twenty-four hours from the onset of an acute scarlatinal nephritis. This is analogous to the stormy onset with initial uremic convulsions that one observes occasionally.

The subacute and chronic types of glomerulonephritis which, from Löhlein's¹³⁵ studies especially, we may feel justified in grouping with the acute inflammations of the kidney are somewhat variable in their effects on blood pressure. I have seen subacute nephritis, with obstinate edema and anemia and a practically constant blood pressure, scarcely ever above the normal. In the chronic cases, with terminal uremic symptoms, the pressure often runs high, though just before death it may show an extreme fall; in one case that I observed the fall was from 240 to 100 mm. during the last twenty-four hours of life. A number of these patients show marked atrophy of the kidney and belong in the group of secondary contracted kidney. Until recently they have not been differentiated from the general group of contracted kidneys. In practically all postmortem statistics they tend greatly to increase the proportion of cases with small kidneys in which marked cardiac hypertrophy has been lacking. Such individuals frequently have dilated and hypertrophied hearts and general dropsy in addition to the uremic symptoms. Roth¹³⁶ has described some of these patients with normal or scarcely increased blood pressure and no changes in the small or large bloodvessels. As a rule the blood pressure rises progressively as serious uremic symptoms supervene.

Uremic hypertension, a hypertensive crisis accompanying the more acute cerebral manifestations, amaurosis, etc., to which Pal¹³⁷ has devoted so much attention, is an undoubted clinical fact. It is in every respect similar to the behavior of the blood pressure in puerperal eclampsia (Vaquez,¹³⁸ Vogeler¹³⁹). Lead poisoning

¹³² Blood Pressure in Scarlet Fever, *British Journal Children's Diseases*, 1912, ix, 444; *Jour. Amer. Med. Assoc.*, 1912, lix, 1829.

¹³³ Ueber das Verhalten des arteriellen Blutdrucks bei den akuten Infektionskrankheiten, *Samml. klin. Vorträge*, 1907, No. 459 (Serie xvi, 9), *Inn. Med.*, No. 138, p. 64.

¹³⁴ Einige Beobachtungen über das Verhalten des Blutdrucks bei Kranken, *Deutsch. Arch. f. klin. Med.*, 1902, lxxiv, 1.

¹³⁵ Ueber Nephritis nach dem heutigen Stande der pathologisch-anatomischen Forschung, *Ergebn. d. inn. Med. u. Kinderh.*, 1910, v, 411.

¹³⁶ Ueber Schrumpfnieren ohne Arteriosklerose, *Virehow's Arch. f. path. Anat.*, 1907, clxxxviii, 527.

¹³⁷ *Gefässkrisen*, Leipzig, 1905.

¹³⁸ Eclampsie puerperale et tension arterielle, *Semaine Médicale*, 1907, xxvii, 121.

¹³⁹ The Blood Pressure During Pregnancy and the Puerperium, *Amer. Jour. Obstet.*, 1907, iv, 490.

may also give rise to analogous symptoms. Briggs¹⁴⁰ has described hypertensive crises in arteriosclerotic subjects. It is such sudden and short-lived accessions of blood pressure that to me most strongly suggest increased activity of the adrenals. The search for epinephrin in the general circulation should be made especially during such periods. Free venesection is the ideal treatment; its effects are shown on the blood pressure chart as clearly as in the behavior of the patient.

Unfortunately I must pass with mere mention the frequent association of increased blood pressure with exophthalmic goitre and uterine fibroids; the development of permanent hypertensive disease in women after the menopause and in many elderly diabetics; the occurrence of symptoms of hyperthyroidism in chronic nephritis. All these are facts suggestive of a relationship between disturbances of the internal secretions and vascular hypertonus, though admitting of far more than one explanation. Perhaps it is well that the limitations of one lecture prevent excursions into this field.

III. CONCLUSIONS. To assemble all the facts, as I have tried to do, is surely one of the most melancholy things in the world as long as these facts remain unrelated. No one cares to look at a pile of bricks and stones, but as soon as these take their places in the structure for which they were shaped and assume those relations which were not seen so long as they remained mere building material, they take on real interest. The first step toward the construction of a scientific theory must always be the assembling of the materials, the next their scrutiny, to see how the parts may be fitted one to the other. The building of the theory comes last, and in the field under discussion must be left for the future. The facts I have outlined, however, impress me as falling logically into certain large groups. In conclusion I shall state my present views about them.

I cannot entirely agree with Krehl¹⁴¹ that, in the main, nephritis as such has no influence on the circulation. To me, heart, arteries, and kidneys seem to stand in an intimate relationship one to the other; the influence of the kidney upon the circulatory system appears as unequivocal as the influence of the circulatory system upon the kidney. A disturbance in either may lead to results, which from the functional standpoint are indistinguishable, though the anatomic pictures be diverse. If the study of experimental nephritis has taught us anything it is this, that the degree and kind of impairment of kidney function can in nowise be inferred from the histologic changes discoverable in the kidney by our present methods.

The symptom of hypertension in renal disease can, I believe, arise in three ways:

¹⁴⁰ Certain Hypertensive Crises in Arteriosclerotic Subjects, AMER. JOUR. MED. SCI., 1905, cxxx, 252.

¹⁴¹ Pathologische Physiologie, Leipsic, 1912, 7th edition, p. 36.

1. Hypertension may arise through purely quantitative reduction of kidney substance below the factor of safety. It is difficult to conceive of this as other than a vascular hypertonus due to retained poisons of some kind. Its clinical paradigm is the hypertension accompanying bilateral ureter obstruction or the unfortunate surgical removal of the only functioning kidney. Possibly it is one factor which helps to produce hypertension in the contracted kidney.

2. Hypertension may arise in connection with the unknown intoxication which causes disturbances of the central nervous system and which we call uremia. This intoxication is not one of retention, in a strict sense, though it is most commonly present in those cases of advanced nephritis which manifest marked nitrogen retention. Clinically it is associated with severe acute nephritis, sometimes at its very onset, besides the subacute and chronic inflammatory affections of the kidney.

3. Hypertension may arise in primary irritability of the vasoconstricting mechanism from unknown, probably extrarenal causes, which lead eventually to arteriolar sclerosis. In this type the disease in the kidney is the sequence, not the cause, of the generalized vascular lesion. When it progresses to a condition of extreme atrophy, resulting in the true primary contracted kidney, a renal element may be added to the existing hypertension. In some cases arteriosclerosis of the larger vessels may spread peripherally and produce a similar form of disease. In these primary vascular diseases it is probable that eventual widespread narrowing of the arterial stream-bed in some cases produces a permanent organic increase in peripheral resistance.

What are the vascular poisons back of these types of hypertensive disease? That question no one can answer. That epinephrin may be one of them is possible; that it is the only one seems to me improbable. One may say the same for the secretion of the hypophysis. I believe it is likely that different poisons produce different types of hypertension. One toxic cause we can name with certainty, lead. Excessive stimulation of the central vasomotor mechanism must also play some part in producing the varied clinical picture.

The first and second types of hypertension may at any time be superimposed upon the third. While the second, the uremic type, must be considered dangerous in itself, hypertension in the arteriosclerotic or atherosclerotic kidney is best regarded as a compensatory effort of the organism, as Bier¹⁴² first suggested, to be interfered with only when danger threatens, either of cardiac failure or of cerebral hemorrhage.

¹⁴² Ueber die Ursachen der Herzhypertrophien bei Nierenkrankheiten, Münch. med. Woch., 1900, xlvii, 527.

In functional pathology, nephritis today presents the aspect of a threefold problem: the problem of edema, the problem of uremia, and the problem of hypertension. The first is well on the road to solution, and in practical therapeutics has lost most of its difficulties. Of the second we have barely scratched the surface. The third, seventy-five years after the first clear statement made by Bright, still baffles our best attempts at solution. That it will yield up its secrets through the increasing application of exact physiologic methods at the bedside and through the discovery of means for reproducing the lesions of chronic nephritis in animals, I confidently believe. Then, and not until then, may we hope for the final merging of morphology and physiology in a higher synthesis. The finished picture of nephritis will appear the same from either aspect; all specialization of function basing itself upon known differentiation of structure, and every alteration of structure manifesting itself by intelligible disturbance of function. It is the task of clinical medicine to effect this final reconciliation, for only the clinician must at all times look at disease from both points of view. In accuracy of observation and refinement of technique the medicine of that day may surpass ours by far more than our laboratories surpass the meagre equipment of Guy's of seventy-five years ago; but the method will still be the method of Richard Bright, the careful comparison of the symptoms studied during life with the lesions found after death.

THE CIRCULATION IN THE ARM OF MAN.¹

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THE circulation in an organ, though dependent primarily upon central conditions, such as the cardiac output and the pressure in the larger veins and arteries, is markedly influenced by the condition of the local bloodvessels. These mainly determine the local blood flow, they regulate the amount of blood held in the organ, and they modify the character of the local arterial pulsations. Few parts of the human body are sufficiently accessible for a study of the local circulation by satisfactory bloodless methods. To this rule, however, the extremities constitute an exception. The arm especially has long been an object of circulatory studies, and within recent years various refinements in older methods and the addition of several new methods have added materially to our

¹ Read at the Cleveland Academy of Medicine, November 15, 1912

knowledge of the circulation in this limb. While the accuracy of the methods available on man is not in general equal to the accuracy of the bloody methods employed on animals, nevertheless the results obtained on man are of peculiar interest. In the first place the radial pulse is so frequently examined by physicians that a broader scientific knowledge of the conditions which may affect this pulse is desirable. Again, the effect which psychic processes exert upon the circulation in a limb can be investigated far better in man than in animals. Finally, many pathological processes can be studied only as they occur naturally in man, and we must turn to patients therefore for a better understanding of these processes and of the effect of treatment upon them.

METHODS. The record of simple volume changes by means of the plethysmograph has been for years our most important method for studying local variations in the arm circulation. Although this method of study has contributed much to our knowledge even within the last few years, nevertheless plethysmograph records suffer from certain inherent defects. For example, they record changes in the arm volume without telling us anything about the circulation at the beginning of an experiment. Furthermore, changes in volume may be due to changes in the caliber of either arteries, capillaries, or veins, and constant and definite relations do not exist between such volume changes and the local blood flow.²

Veiel³ has recently restudied the radial pulse. For this purpose he used the mirror recorders of O. Frank, which follow the details of the curves with great precision. Space will not permit a review of this work, but I will mention in passing that these and similar studies⁴ have shown that the finer details of the radial pulse and even of the brachial pulse, differ greatly from those of the aortic and the carotid pulses. They are in fact peripheral pulses, and their form depends largely upon the condition of the local arteries. We⁵ are now engaged in a study of the volume pulse of the arm and of the flow pulse in the brachial artery by means of the mirror recorders of Frank. The volume pulse of the arm, obtained from a plethysmograph, records the difference between the varying entrance of arterial blood and the constant or nearly constant exit of venous blood. If, for example, 2 c.c. of blood enters the plethysmograph by way of the artery with the primary pulse wave and at the same time $\frac{1}{4}$ c.c. leaves by way of the veins, then the swelling which is recorded as the volume pulse would amount to $1\frac{3}{4}$ c.c.

² V. E. Henderson, and O. Loewi, Ueber die Wirkung der Vasomotorenreizung, Arch. f. exp. Path. u. Pharm., 1905, liii, 56.

³ Ueber die Bedeutung der Pulsform, Deut. Arch. f. klin. Med., 1912, cv, 249.

⁴ O. Müller and E. Weiss, Ueber die Topographie, die Entstehung, und die Bedeutung des menschlichen Sphygmogrammes, Deut. Arch. f. klin. Med., 1912, cv, 320.

⁵ A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, Trans. Assoc. Amer. Phys., 1912.

If the veins are momentarily obstructed, or if the normal venous outflow is known, then the volume pulse becomes (or can be translated into) a record of the arterial inflow at each point of the pulse cycle. We shall speak of this as the flow pulse of the brachial artery, for most of the blood enters the portion of arm studied through this channel.

The tachograph of von Kries⁶ attempts to record the variations in the velocity of the arterial blood stream to the arm, but it does not record the constant upon which these variations are superimposed.⁷ Similar velocity curves may be derived by the method of Fick⁸ from volume curves, and with present methods they should be more perfect technically.

Two methods for estimating the blood flow in the arm or hand of man have been recently described. The first of these, which we have mostly used is based upon a principle described by Brodie and Russell,⁹ and will be spoken of as the plethysmographic method.¹⁰ The patient lies in a reclining or semi-reclining position and the slightly elevated arm is placed in a plethysmograph, which is connected with a volume recorder. A narrow pressure cuff, similar to that used for determining blood pressure, is then placed about the arm, just outside of the plethysmograph. While the volume of the arm is being recorded the pressure in the cuff is suddenly raised to about the diastolic arterial pressure by opening a valve that places the cuff in communication with a large bottle containing air under pressure. The pressure in the cuff obstructs the veins, but leaves the arteries open. For a short time therefore the blood flows freely into the arm, but cannot escape. At this time the swelling of the arm, as indicated by the volume recorder, corresponds to the normal rate of arterial inflow. Naturally only the first portion of such a record can be used: (1) because the inflow is soon obstructed by the collection of blood in the veins and capillaries, and (2) because the rising venous pressure will eventually force blood beneath the obstructing cuff. The operation of these factors causes a gradual lessening in the rate of arm swelling, which is apparent on the tracings. The longer the period of a constant rate of swelling the greater the reliance that one may place on the accuracy of a given record. In order to increase the reservoir in which blood may collect without raising the pres-

⁶ Studien zur Pulslehre, Freiburg, 1892.

⁷ J. von Kries, Ueber die Methoden zur Beobachtung der arteriellen Blutströmung beim Menschen, *Zeitschr. f. exp. Path. u. Therap.*, 1911, ix, 453; Christen, Tachogramm. Pulsvolumen. und Schlagvolumen, *Zeitschr. f. exp. Path. u. Therap.*, 1911, ix, 607.

⁸ Gesammelte Schriften, Würzburg, 1904, iii, 550.

⁹ On the Determination of the Rate of Blood Flow Through an Organ, *Jour. Phys.*, 1905, xxxii, p. xlvii.

¹⁰ A. W. Hewlett and J. G. Van Zwaluwenburg, The Rate of Blood Flow in the Arm, Heart, 1909, i, 87. (The use of "we," etc., throughout this paper refers to work done by the author, either alone or in collaboration with other members of the staff in the Department of Internal Medicine, University of Michigan.)

sure in the vessels, a slight elevation of the arm, which tends to empty the veins, is of considerable technical importance.

The second method for determining the blood flow in the hand is that described by G. N. Stewart.¹¹ As it involves a measurement of the amount of heat given off from the hand in a calorimeter, it will be referred to as the calorimetric method. This method depends upon the principle that the heat thus given off is derived almost entirely from the blood that circulates through the hand. Knowing (1) the amount of heat given off from the hand, and (2) the temperature of the blood which enters and that which leaves the hand, one may calculate how much blood may have passed through in order to give off the heat eliminated.

PSYCHIC EFFECTS. Over thirty years ago, A. Mosso¹² showed that increased attention and mental work caused a diminution in the volume of the arm and in the size of the volume pulse. These observations have since been confirmed and extended by numerous investigators,¹³ and the relation of these volume changes to those occurring in other parts of the body, as well as their relation to the different types of psychic stimuli, have been repeatedly studied. According to Weber the following changes in the distribution of blood in the body occur as a result of mental or emotional activity.

WEBER'S TABLE.

	Brain.	External head.	Abdominal organs.	Limbs and external trunk.
An impulse to motion with or without execution of the movement	+	—	—	+
Mental work	+	—	+	—
Terror (surprise)	+	—	+	—
Pleasure	+	+	—	+
Unpleasant sensations	—	—	+	—
Sleep	+	—	—	+

+ indicates an increase and — indicates a diminution in the content of blood in the part.

It will be seen that most emotional and mental processes, with the exception of pleasurable sensations, are associated with temporary decreases in the arm volume. These changes are accompanied by changes of a similar character in all the extremities and in the surface of the trunk and by changes of an opposite character in the volume of the abdominal organs—a reciprocal relation which is rather general, and is known as the Dastre-Morat Law. The above changes in arm volume are usually associated with corresponding changes in the size of the volume pulse.

¹¹ The Measurement of the Blood Flow in the Hands, Heart, 1911, iii, 33.

¹² Die Diagnostik des Pulses, Leipzig, 1879.

¹³ A. Lehmann, Elemente der Psychodynamik, Leipzig, 1905. E. Weber, Der Einfluss psychischer Vorgänge auf den Körper, Berlin, 1910.

These psychic vasomotor changes also affect the blood flow through the arm. When the subject's attention or interest was aroused we have repeatedly observed a sudden reduction in blood flow, which might amount to 30 per cent. or more; and such sudden changes have occasionally proved confusing when the effect of other factors upon the blood flow in the arm was being studied. These sudden changes in blood flow are particularly marked in young and neurotic individuals.

EFFECT OF EXERCISE. Since the experiments of Chauveau and Kaufmann¹⁴ on the horse it has been known that the voluntary use of muscle is associated with a marked acceleration of the local blood flow, the increase in the experiments of these investigators being from four to nine times the resting flow. Volume changes in the arm of man during local exercise are difficult to measure by the plethysmograph, because the exercise disturbs the tracings; but direct measurements of the arm volume before and after exercise show increases in volume, which may amount to 200 c.c.¹⁵ The rate of the blood flow in the arm of man is certainly markedly increased, for we¹⁶ found the flow from three to eight times the normal immediately following local exercise, and Stewart obtained a definite increase for the hand in one experiment.¹⁷

Muscular contractions produced in animals by stimulation of the local nerves seem to be much less effective in accelerating the local blood flow.¹⁸ Massage causes no arm swelling.¹⁹ It would seem that the local circulatory changes are due only in small part to the mechanical effect of the muscular contractions; in the main they are due to vasomotor effects associated with the normal voluntary innervation of the muscles sent out from the higher nerve centres, for Weber²⁰ has shown that marked swelling of the arm may be induced in a motionless person during hypnotic sleep merely by the suggestion of motion in this arm.

Exercise of one arm has but little effect upon the blood flow in the other motionless arm. We have²¹ found no change or a slight increase, and Stewart²² found a moderate diminution. In Weber's experiments during hypnosis the volume of the opposite arm changed but slightly—sometimes in one direction and sometimes in the other. Vigorous exercise, with rise of blood pressure

¹⁴ *Compt. rend. de l'Acad. des sciences*, 1887, civ, 1126.

¹⁵ Rancken, Ueber die Volumenverhältnisse des Armes bei Massage, aktiver Muskelarbeit und lokalem Heissluftbade, *Skan. Arch. f. Physiol.*, 1910, xxiii, 55.

¹⁶ A. W. Hewlett and J. G. Van Zwaluwenburg, *loc. cit.*

¹⁷ G. N. Stewart, *loc. cit.*

¹⁸ J. A. Tschewsky, Ueber die Aenderung des Blutstroms im Muskel bei tetanischer Reizung seines Nerven, *Arch. f. d. gesamt. Physiol.*, 1903, xevii, 289; R. Burton-Opitz, Muscular Contraction and the Venous Blood Flow, *Amer. Jour. Physiol.*, 1903, ix, 161.

¹⁹ Rancken, *loc. cit.*

²⁰ *Loc. cit.*

²¹ A. W. Hewlett and J. G. Van Zwaluwenburg, *loc. cit.*

²² G. N. Stewart, *loc. cit.*

and warming of the body, will, however, increase the flow in an unused extremity. For example, immediately after violent exercise on the stationary bicycle the blood flow in the arm is considerably increased, but it falls with the fall of blood pressure, and the final level may be but little different from the original. In some individuals, however, the final level is somewhat raised due presumably to the warming effect of exercise.

THERMIC EFFECTS. The circulation in the arm is exceedingly sensitive to thermic influences, whether acting upon the local skin surface or upon some distant part of the body. When subjected to heat the arm becomes larger and softer, the skin becomes warm moist, and often reddened, the arteries feel large and soft, and the veins stand out prominently. All methods of study show that when heat is applied to the arm the bloodvessels tend to relax. The swelling of the arm may amount to 70 c.c.,²³ the volume pulse becomes larger,²⁴ the tachogram higher,²⁵ the blood flow may be increased from three to eight times the original,²⁶ and the venous pressure rises. If the application of heat causes pain there may be a temporary constriction of the vessels of the arm, owing to the psychic effect of the pain, following which the usual dilatation occurs. After the arm has been exposed for some time to high temperatures there is a tendency for the vessels to remain dilated and the blood flow rapid, even though the arm is subsequently somewhat cooled. It has been maintained, though to my mind not proven, that a paresis of the vessels exists in such cases.²⁷ Mild degrees of burn, as indicated by local reddening, which persists for days, are certainly due to a paralytic hyperemia, affecting chiefly the skin capillaries.

When the arm is exposed to local cold it tends to shrink. Gloves and rings fit more loosely, the skin feels cold and is pale or cyanotic, the radial artery is small and hard, the cutaneous veins become smaller or may disappear, the tachogram and volume pulse lessen in size, and the blood flow diminishes to one-fourth of the normal or even less. When the cold is intense and continued for some time the volume of the arm may again increase slightly,²⁸ and somewhat more heat is said to be given off from the hand at such extreme temperatures.²⁹ In most persons, however, we have been unable to obtain an increased blood flow during exposures to water sufficiently cold to cause considerable pain. The skin cyanosis and

²³ Rancken, loc. cit.

²⁴ A. Mosso, loc. cit.

²⁵ Balli, Ueber den Einfluss lokaler und allgemeiner Erwärmung und Abkühlung der Haut auf das menschliche Flammentachogramm, Dissertation, Bern, 1896.

²⁶ A. W. Hewlett, J. G. Van Zwaluwenburg, and M. Marshall, The Effect of Some Hydrotherapeutic Procedures upon the Blood Flow in the Arm, Arch. Int. Med., 1911, viii, 591.

²⁷ Ibid.

²⁸ U. Mosso, L'action du chaud et du froid sur les vaisseaux sanguins, Arch. ital de biol., 1889, xii, 346.

²⁹ Robinson and Stiles, External Temperature and Cutaneous Blood Flow, Amer. Phys. Ed. Rev., May, 1909.

swelling during exposure to cold can be explained as due to dilatation of the cutaneous capillaries and venules with edema without there being necessarily a dilatation of the smaller arterioles which chiefly govern the blood flow.

Changes in the room temperature markedly influence the blood flow in the arm. Variations of 50 per cent. in the flow may be produced by changes in room temperature³⁰, even when the subject feels subjectively comfortable. The variations produced by chilliness on the one hand to beginning perspiration on the other will cause variations in the flow through the arm that may amount to seven to ten times. The relation of these changes in the flow to the flow pulse of the brachial is interesting and instructive. Ordinarily most of the blood enters the arm through the brachial artery during the primary systolic pulse wave, and but little enters during the remaining portion of the pulse cycle. In a set of experiments on a normal individual³¹ it was found that during exposure to a cold room the primary pulse wave was diminished about proportionally to the diminished flow, and that the main entrance of blood still occurred during the primary systolic wave. Approximately the same relation held during warming of the room up to moderately increased rates of blood flow. When the flow became very rapid, however, the size of the primary wave did not increase. At this time a continued rapid flow occurred throughout the entire pulse cycle. Apparently the large arteries had reached a maximum size, but the smaller arteries, which mainly govern the flow, had continued to dilate and allowed a rapid continuous stream to pass through them.

Thermic stimuli in addition to producing local changes in the circulation also influence the circulation in distant parts of the body. In general the application of heat or cold to one extremity causes a volume change in the same direction in the other extremities, and a volume change in the opposite direction in the abdominal organs.³² Stewart³³ has shown that these vasomotor reflexes also affect the blood flow in the hand, and that they may be conveniently studied by plunging one hand in hot or cold water while the flow in the other is being recorded. The application of heat or cold to the interior of the stomach will cause a variation in volume of the extremities in the opposite direction from the effect of heat or cold applications to the skin (Müller³⁴). Although the two arms tend to vary in the same direction it is possible when one

³⁰ A. W. Hewlett, *The Effect of Room Temperature upon the Blood Flow, etc.*, Heart, 1911, ii, 230.

³¹ A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, loc. cit.

³² O. Müller, *Blutverteilung im menschl. Körper unter den Einfluss thermischer Reize*, Deut. Arch. f. klin. Med., 1905, lxxii, 547.

³³ The Effect of Reflex Vasomotor Excitation on the Blood Flow in the Hand, Heart, 1911, iii, 76.

³⁴ Loc. cit.

is exposed to cold and the other to heat for the flow to be slow in the former and fast in the latter.

It is evident, therefore, that thermic applications produce marked variations in the circulation in the arm, and that they may do this either through direct action or through distant reflexes. To what extent slight variations in the temperature of the blood may influence the peripheral blood flow through an action on the medullary centres has not been accurately determined for man. We know that in animals such action may occur,³⁵ and there is suggestive evidence that the temperature of the blood may be an important factor in the normal vasomotor control of man.³⁶ We have noticed repeatedly that when the body temperature has been somewhat reduced the blood flow through the arm tends to fall under slight provocation even though the local circulation had been fairly good previously.³⁷ Also, the general experience in hydrotherapeutic institutes has emphasized the importance of preventing heat losses sufficient to lower the body temperature when attempting to get a good reaction following cold procedures.

OTHER PHYSIOLOGICAL FACTORS. In addition to the effect of the psychic processes, exercise, and thermic influences it seems to us probable that other physiological factors may influence the blood flow in the arm of man, for in our experience the rate may vary considerably on different days even though the room temperatures are carefully controlled. As yet, however, we do not know the exact nature of these factors.

THE ARM CIRCULATION IN DIFFERENT INDIVIDUALS. The blood flow in the arm varies considerably in different individuals. In our first paper³⁸ we stated that the flow usually lay between 2 c.c. and 4 c.c. of blood flow per 100 c.c. of arm substance per minute. A wider experience, however, has caused us to modify these figures. In our original experiments the subjects were usually stripped to the waist and the room was often somewhat chilly, both of which factors would tend to lessen the flows. At present we regard the usual variations of blood in the arms of normal individuals as from 2 c.c. to 8 c.c. of blood flow per 100 c.c. of arm substance per minute, while for a given individual variations of 50 per cent. are not uncommon. Stewart's figures for the hand varied from 3.5 c.c. to 14 c.c. of blood flow per 100 c.c. of hand substance per minute, while the variations in a given individual were insignificant. We have shown that this difference in rates as obtained by the two methods also holds on a single individual,³⁹ the caloric method

³⁵ Kahn, Ueber die Erwärmung des Carotidenblutes, *Arch. f. Anat. u. Physiol. Physiol.*; 1904, Abteil. Supplemental Band, p. 81.

³⁶ R. Stein, *Zeitschr. f. klin. Med.*, 1892, xx, 63.

³⁷ A. W. Hewlett, J. G. Van Zwaluwenburg, and M. Marshall, *loc. cit.*

³⁸ A. W. Hewlett and J. G. Van Zwaluwenburg, *loc. cit.*

³⁹ A. W. Hewlett and J. G. Van Zwaluwenburg, Comparison Between the Blood Flow in the Arm and in the Hand, *Proc. Soc. Exp. Biol. and Med.*, 1911, viii, 111.

usually giving a more rapid blood flow in the hand relative to its volume than does the plethysmograph method for the arm, and we are inclined to attribute these differences to an actual difference in the circulation, the flow in the hand relative to its volume being greater than in the arm.

When we compare pathological individuals under ordinary conditions with these normal standards we usually find that their blood flows in the arm or hand fall within the normal limits of variation. This rule holds for such conditions as severe anemia, hypertension, and heart disease except in the stage of badly broken compensation. Slow rates are associated in general with cold extremities. The slowest that I have encountered was in a patient with dead fingers in whom the flow was 0.7 c.c. of blood flow per 100 c.c. of arm substance per minute. Stewart also found a slow flow in this condition. The most rapid flows are encountered in those with warm extremities, and of these patients with severe types of Graves' disease show the fastest rates. The most rapid rate that we have encountered under ordinary conditions of room temperature was 19 c.c. of blood flow per 100 c.c. of arm substance per minute.

During continuous fever the blood flow in the arm usually lies within the normal limits of variation. To what extent it differs from what would be the usual flow for the individual studied has not been determined. When the temperature is rising during fever the blood flow in the arm is relatively slow,⁴⁰ and during a chill the volume pulse becomes decidedly smaller.⁴¹ When the temperature is falling, on the other hand, the flow is relatively fast and the volume pulse is large.

In general the size of the volume pulse in different individuals corresponds fairly well to the rate of blood flow in the arm, the larger the pulse the more rapid the flow, etc. The main entrance of blood into the brachial artery occurs during the primary systolic pulse wave, after which there is little or no flow. We have already pointed out that when an individual is very warm this relation does not hold, for the flow is then increased out of proportion to the increase in the primary wave and the blood enters the arm rapidly throughout all portions of the pulse cycle. This was found to be true also during muscular exercise and in the rapid flows of severe Graves' disease. In aortic insufficiency the opposite condition may hold. The volume pulse in typical cases is unusually large,⁴² and following the primary wave an evident back flow throughout the remainder of the pulse cycle is sometimes but not always present. More blood, therefore, may enter the brachial artery during the primary wave than flows through the arm during the whole pulse cycle. This back flow in the brachial is not, however,

⁴⁰ A. W. Hewlett, loc. cit.

⁴¹ A. Mosso, loc. cit.

⁴² A. W. Hewlett and J. G. Van Zwailenburg, unpublished observations.

characteristic of aortic insufficiency. As we shall see a short wave of backflow is evident in the nitroglycerin pulse, and probably occurs to a lesser extent under other circumstances. It seems possible also to have a slight continuous backflow in other conditions.

VASCULAR REACTIONS IN DISEASE. The normal response of the vessels of the arm to psychic and thermic stimuli may be modified during disease. Two methods have been used for studying these abnormal vasomotor reactions. In the first, plethysmographic records are taken while the individual is subjected to some stimulus, such as mental work, pain, or the application of heat or cold to the skin. According to the second the blood flow is determined in one hand while the opposite hand is thrust into hot or cold water.

Weber⁴³ who has made a special study of psychic processes, found that there was a tendency for the usual vasomotor reflexes associated with attention, and the suggestion of movement to be lessened or even to be reversed during mental or physical fatigue. The reflexes normally produced by pleasant or unpleasant stimuli, on the other hand, were usually unaffected during fatigue. He states also that patients with Graves' disease, neurasthenia, or hysteria often showed such fatigue phenomena more readily than do normal individuals, and that in some of these patients this diminution or reversal of the normal reflexes was constantly present.

The vasoneuroses of which Raynaud's disease may be taken as a type have been studied by Curschmann, Simons, and Stewart. It is generally agreed that such patients usually show abnormal variations in their vasomotor reflexes. As yet, however, there is no general agreement as to character or constancy of these variations. Curschmann⁴⁴ found an abolition of the plethysmograph reactions to thermic and to various psychic stimuli. Simons⁴⁵ found variable reactions at different times and a lack of symmetry in the reaction on the two arms. Stewart⁴⁶ found a transient reaction to cold followed by an increase in the blood flow. It would seem not unlikely that such patients show considerable variations among themselves, and that a given individual may show different reactions at different times.

Organic lesions of the nerves or of the central nervous system may also affect the vasomotor reactions of the extremity. Simons⁴⁷ found that the vascular reactions of the hand depended upon an intact condition of the median and ulnar nerves and was inde-

⁴³ Loc. cit.

⁴⁴ Untersuchungen über das funktionelle Verhalten der Gefäßen bei trophischen und vasomotorischen Neurosen, Münch. med. Woch., 1907, liv, 2519.

⁴⁵ Plethysmographische Untersuchungen der Gefäßreflexe bei Nervenkranken, 11, Arch. f. Anat. u. Physiol., Physiol-Abteil, 1910, Supplemental Band, 429.

⁴⁶ Loc. cit.

⁴⁷ Plethysmographische Untersuchungen der Gefäßreflexe bei Nervenkranken, 1, Arch. f. Anat. u. Physiol., Physiol-Abteil, 1910, 557.

pendent of the conditions of the radial nerve. Stewart found a transient reaction in patients with neuritis and an abolition of reactions in an old hemiplegic hand.

Arteriosclerosis, as shown by Romberg and his school⁴⁸ also tends to abolish the reflexes produced by the application of ice to the upper arm. It is interesting, however, that a thickened radial artery, especially in continuous hypertension, may show a normal or increased reaction. In such cases it may be assumed that the thickening is due to a hypertrophic muscle which shows normal or increased reactive power. In advanced heart disease the vascular reactions may be absent.⁴⁹

THERAPEUTIC EFFECTS. Thus far we have accumulated relatively few data concerning the effect of drugs upon the circulation in the arm. It seems certain, however, that the most effective measures at our disposal for influencing this circulation are thermic stimuli applied either locally or to some distant part of the body. Skin irritants, such as mustard, produce a local dilatation of the cutaneous capillaries and venules, but their action upon the blood flow through the part, aside from thermic effects, is relatively slight.⁵⁰ One may reconcile these observations by assuming that the chief factor controlling the blood flow is the state of contraction of the small arterioles, and that mustard produces a dilatation of the cutaneous capillaries and venules without a corresponding dilatation of the underlying arterioles.

The intravenous injection of strophanthin⁵¹ or digalen⁵² in therapeutic doses affects neither the volume of the arm nor its normal reaction to the application of cold. Such injections are said, however, to affect the tonus of the larger arteries.⁵³ Intravenous injections of caffeine diminish the arm volume and intravenous injections of sodium nitrite increase it.⁵⁴ We have found that medicinal doses of nitroglycerin dropped on the tongue produce definite changes.⁵⁵ Within a few minutes the arm volume increases and the volume pulse becomes larger. The pulsations of the brachial artery as obtained by the Erlanger sphygmomanometer also become larger. The blood flow through the arm is not greatly affected. The flow pulse shows that a large arterial wave enters the arm and that

⁴⁸ Romberg and Müller, Ueber Bedeutung und Technik der plethysmographischen Funktionsprüfung gesunder und Kranker Arterien, *Zeitschr. f. klin. Med.*, 1912, lxxv, 93.

⁴⁹ G. N. Stewart, loc. cit.; Romberg and Müller, loc. cit.

⁵⁰ C. I. Wood and P. G. Weisman, The Effect of a Skin Irritant on the Local Blood Flow in the Hand, *Arch. Int. Med.*, 1912, x, 196.

⁵¹ O. Vagt, Ueber die Herz und Gefäßwirkung des Strophanthins bei gesunden und kranken Menschen, *Med. Klinik*, 1909, v, 1858.

⁵² H. Eychemüller, Ueber die Herz und Gefäßwirkung der Digalens bei gesunden und kranken Menschen, *Berl. klin. Woch.*, 1909, xvi, 1677.

⁵³ Nägels, *Zentralbl. f. Herz. und Krankheiten*, 1910.

⁵⁴ O. Müller, Ueber die Herz und Gefäßwirkung einiger Digitaliskörper bei gesunden und kranken Menschen, *Verhandl. des. Kongr. f. in. Med.*, 1909, xxvi, 364.

⁵⁵ A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, loc. cit.

it is in large part immediately reflected. We have assumed in such cases a marked relaxation of the larger arteries of the arm, which allows a large pulse wave to enter, while at the same time the finer arterioles are contracted and do not allow the blood to flow through them. Owing in part to the relaxed condition of the large arteries the wave is reflected from the periphery.

CONCLUSIONS. In studying the local circulation in the arm of man, local conditions must be kept constantly in mind. The tachogram, the volume pulse, and the finer waves of the radial pulse depend in large part upon the condition of the larger arteries. The blood flow and the temperature of the part depend largely upon the condition of the finer arterioles. The color of the part depends in part upon the condition of the cutaneous capillaries and venules and in part upon the local flow. Changes in any of these cannot be referred unreservedly to changes in the heart action.

Many changes in the local circulation can be referred to thermic effects, and the function of the skin in serving as a physical means of heat regulation must be borne constantly in mind. Conditions of chilliness or warmth, whether occurring as a result of external temperature or as a result of fever, influence most markedly the peripheral circulation in the extremities. If we wish to increase the circulation in an extremity the most effective means at our disposal are general and local warmth. In comparison with these thermic measures the effect of drugs is insignificant.

AN INSTANCE OF PREMATURE BEATS ARISING IN THE AURICULOVENTRICULAR BUNDLE OF A YOUNG CHILD.

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E. H., a child, aged four and a half years, has been under observation for eighteen months or more, and whenever examined has shown premature beats of a curious but constant type.

Family History. Both parents are living and well. The mother has had at least one attack of rheumatism. Three sisters and brothers are living and well.

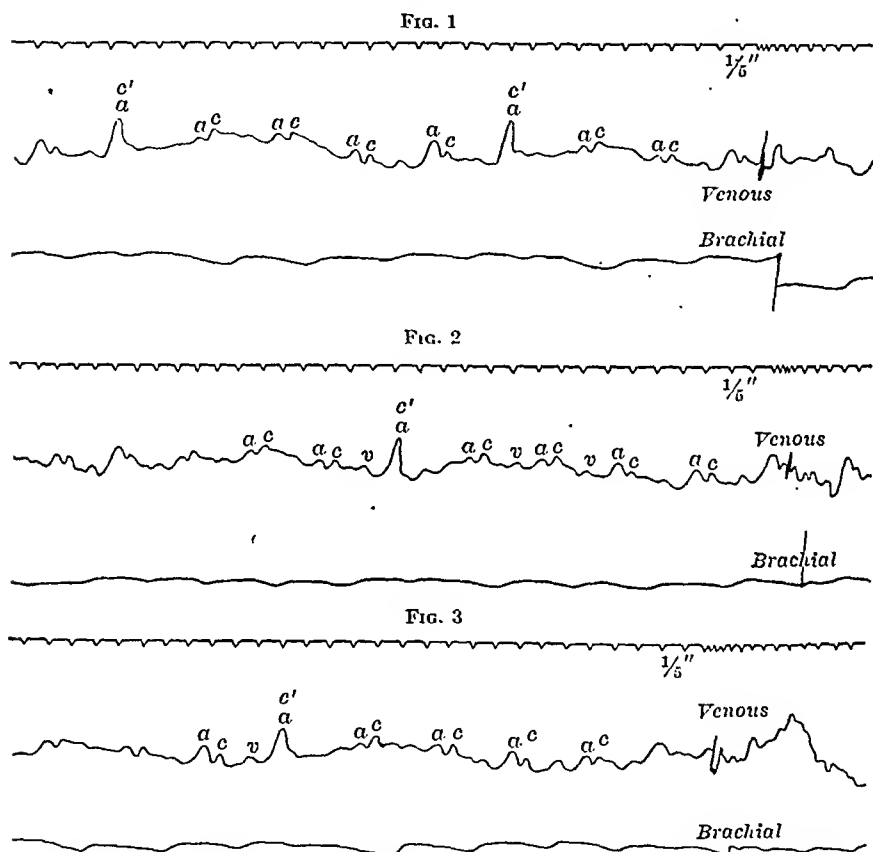
Previous Illness. As a baby had chickenpox. In November,

1910, had a severe attack of measles, lasting about four weeks. No history of rheumatic infection or other illness.

Examination shows a child somewhat small for his years, but apparently quite healthy. Is able to play and to get about without any evident cardiac distress.

Heart: Percussion outline normal. Sounds are everywhere clear. The normal rhythm is interrupted by moderately frequent premature contractions, each of which is accompanied by two heart sounds.

No abnormalities are detected in the other organs.



FIGS. 1, 2, and 3.—Simultaneous tracings from the brachial and jugular pulses, each showing one or more premature beats.

Description of graphic records: In *polygraphic curves* (Figs. 1, 2, and 3) a slight degree of sinus arrhythmia is evident, and this rhythm is interrupted from time to time by premature beats, which, allowing for the sinus arrhythmia, are followed by compensatory pauses. Each rhythmic radial beat is accompanied in the venous tracing by *a*, *c*, and *v* waves, as seen in the accompanying tracings. At the occurrence of a premature beat a large composite wave is seen in the jugular tracing, occurring at or a little before the expected time of a *c* wave, and also at the expected

instant for the rhythmic auricular wave. The tall composite wave is evidently due to a simultaneous contraction of auricle and ventricle, the ventricular contraction being premature while the auricular contraction belongs to the normal series of such beats. The polygraphic pictures are consequently typical examples of premature contractions arising in the ventricle, disturbing the ventricular rhythm, while the auricular rhythm remains undisturbed.

Electrocardiographic curves show the same events quite clearly. Examples of the three leads are shown in Figs. 4, 5, and 6. In each of these curves two or three premature beats are seen. In lead *I* (Fig. 4) there are three such beats. They resemble the normal ventricular beats except that *R* is shorter, *S* deeper, and *T* somewhat taller. The rhythmic auricular contraction falls in

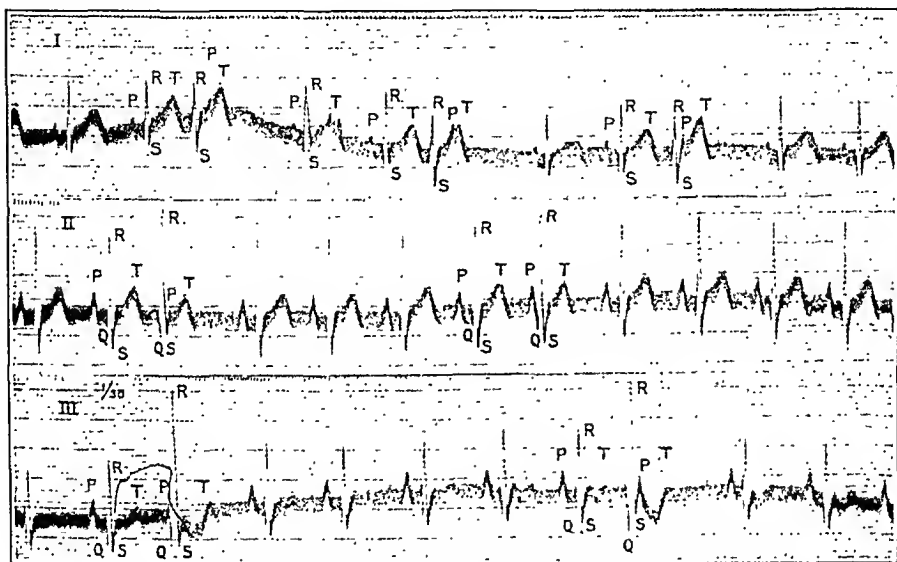


FIG. 4

FIG. 5

FIG. 6

FIGS. 4, 5, and 6.—Electrocardiograms from the same case showing the three leads: lead *I*, from right arm to left arm; lead *II*, from right arm to left leg; lead *III*, from left arm to left leg.

each instance on the upstroke of *T*, but the relation of the buried *P* summit varies somewhat in relation to the apex of *T*, being near its summit in the central disturbance and near its onset in the last disturbance. In lead *II* (Fig. 5) there are two premature beats. The ventricular complexes of these beats have a similar form to the rhythmic beats except that *R* is taller and *Q* is deeper, while *T* is somewhat reduced. The sequential auricular contraction falls with *S* in the case of the first premature beat. In lead *III* (Fig. 6) there are two premature beats, the ventricular complexes of which have tall *R* summits, deep *Q* deflections, and inverted *T* summits, as compared with the sequential beats. The sequential *P* falls directly before and with *Q* of the first premature beat, and with and directly after *S* of the second premature beat.

The electrocardiograms therefore show the ordinary events as they are recognized in premature ventricular contractions so far as the relationship of separate auricular and ventricular contraction is concerned. The peculiarity of the curves lies in the resemblance between the ventricular complexes of the premature beats and those of the rhythmic beats of the same case. This resemblance is so close that the premature beats can only have arisen in impulses which have passed along the normal channels of conduction which join auricle to ventricle. They are beats which are known to be of supraventricular origin, meaning by this term beats propagated from impulses arising above the level of the main division of the auriculoventricular bundle. The minor alterations in the shapes of the complexes in the three leads, changes which have been already described, are not incompatible with this view, for similar changes are known to occur when premature beats arise in the auricle. The changes result from prematurity, and in a measure are comparable to those which are seen with changes of heart rate; they have been described with other phenomena of a similar character under the term "aberration."

The premature beats of the present case, though arising above the main division of the bundle, have not interfered with the sequential contractions of the auricle; it may consequently be presumed they have arisen at a lower level than the main mass of auricular tissue; in other words, either in the auriculoventricular node or in the main bundle itself. If these beats arose in the auriculoventricular node we should anticipate simultaneous contractions of auricle and ventricle propagated from this point. But, as a matter of fact, and as the curves show, synchronism of contractions when it does occur is a coincidence, for the auricular beats evidently originate in the normal impulse centre, the sino-auricular node, while the ventricular beats come from an extraneous point.

There seems only one possible objection to the interpretation of these contractions as having their origin in the bundle itself. If they arose in the auriculoventricular node at such instants that the impulse sent back to the auricle always found this chamber in the refractory state, then the auricle would not contract in response to the nodal impulse and the synchronism of the auricular and ventricular beats might be readily explained. But, as a matter of fact, this explanation will not suffice in the case of the present figures. If we take the time for the retrograde impulse at the same length as the *P-R* interval, then in the case of Fig. 4 the impulse of the central premature beat should have reached the auricle before it contracted in response to the impulse from the pacemaker; on the other hand, allowing the same interval, the retrograde impulse would not reach the auricle in the case of the last premature beat of Fig. 5 until the sequential auricular systole was completed.

And it is a matter of indifference what length of time is allowed for the retrograde impulse, for whatever the length the explanation of the transmission of such impulse would break down in the case of one or other of the premature beats considered. We are therefore forced to the conclusion that the premature contractions arose at a point so far distant from the auricle that (as in the case of the interpolated ventricular contractions) no impulses are sent backward to the auricle. Presumably such a point is to be found at a lower level than the auriculoventricular node, and, as we have already concluded from the shape of the premature ventricular complexes that they arose above the level of the main division we must perforce locate the point of origin in the main stem of the bundle.

Another example of beats of the same sort, though perhaps the instance was less clear, was described in the *Quarterly Journal of Medicine*, October, 1911, v, p. 1, No. 17.

Summary. An instance of premature contractions is described in a child, aged four and a half years; the point of origin of the beats was probably to be located in the main stem of the auriculo-ventricular bundle.

THE PROBLEM OF THE ALIEN INSANE.¹

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A DEFINITION of the word "problem" is "a matter difficult of solution or settlement." Certainly in the latter sense it is difficult of settlement if not of solution, and the question of the alien insane may be considered a problem.

Nowhere in the civilized world does so anomalous a condition exist as regards the insane as in the United States, due in the main, as we shall see, to the inadequacy of the Federal laws, both as to the admission of immigrants and the deportation of insane aliens. Five years' actual residence at least, from the date of admission into this country are required before an alien can become a citizen, yet the law as to his deportation, even though he has never given any evidence of a desire to become a citizen; even though he be incurably insane; even though he is a public charge, says, under Subdivision 3 of Rule 22 of the Department of Commerce and Labor, Bureau of Immigration and Naturalization, that the State of New York must present an application which, among other

¹ Read at the Two Hundred and Forty-ninth Regular Meeting of the Society of Medical Jurisprudence of New York City, Monday, December 9, 1912.

things, shall be accompanied by a medical certificate containing the following:

“(a) An explicit statement that the alien is a public charge, where and how, and, if in an institution, the date of admission thereto.

“(b) A full and accurate statement of the alien’s disabilities, mental or physical; also whether or not a complete cure is possible; and if yes, when; and if not, whether partial cure may be expected; and to what extent the alien will thereafter be self-supporting. Also, in insane cases, recovered or apparently recovered from the attack, whether new attacks are to be expected.

“(c) Whether or not the disabilities described constitute the sole causes why the alien is a public charge; any other causes to be stated.

“(d) Whether the causes which render the alien a public charge existed prior to landing or arose subsequent thereto, and in the former case the reasons in detail justifying such a conclusion.

“Where the bureau so directs, the application must be further accompanied by a complete copy of the clinical or general history of the case as shown by the hospital records, including the statements of relatives and friends. If deemed advisable by the local immigration officer, it may be further accompanied by the certificate of an officer of the Public Health and Marine Hospital Service in relation to the alien’s condition.”

This rule is based upon the immigration laws of the United States, which further provide that the alien *may not be deported at all* if he has been in this country for a period of three years or more, the State of New York being then obliged to care for this alien for the rest of his natural life, notwithstanding the possible as well as probable fact that he may not have been a resident of the State but a very short time. In short, while it takes five years for an alien to become a citizen, he can, by being within the borders of the United States for three years, and at no time in any way contributing to the support of the Commonwealth, be in a position to compel the State of New York or any other State to maintain him during the remainder of his life.

The ordinary procedure, as we can readily see, makes it fairly difficult for the State of New York to rid itself of undesirable aliens, even when a common-sense point of view is taken of the meaning of the law. It seems, however, that it was not sufficiently difficult in the eyes of the Department of Commerce and Labor, so a rule was promulgated known as “Decision No. 120.” This decision was rendered by Charles Earl, solicitor of the Department of Commerce and Labor, January 11, 1912; later (February 3, 1912) approved by Attorney-General Wickersham. The history of this decision is to be found in the report of the Bureau of Deportation for the year ending September 30, 1912, and in brief is as follows:

"The decision referred to an insane alien at the Manhattan State Hospital who has been certified to by this bureau as becoming a public charge on account of insanity. The certificate set forth that her mental disease resulted from causes existing prior to landing, such causes being constitutional psychopathic tendencies, mental instability, and deficiency, and was endorsed by a passed assistant surgeon of the Public Health and Marine Hospital Service, who certified that in his opinion the patient was insane from predisposing causes existing prior to landing, and that his opinion was based upon a careful examination of the alien, the history of the case, and the records on file at the institution. Furthermore, an independent examination on the part of the Commissioner of Immigration at Ellis Island by a lay immigrant inspector corroborated the details of the history, and, as the result of the combined examination on the part of the passed assistant surgeon of the Public Health and Marine Hospital Service, the medical members of this bureau and the lay immigrant inspector attached to the immigration station at Ellis Island, the Commissioner of Immigration recommended the deportation of this alien in accordance with the laws. The honorable solicitor who, we are led to believe, can make no claim to either any general medical education or any knowledge of what pertains to the diagnosis of mental incapacities, examined the same medical records and the testimony of the various alienists, both State and Federal, and arrived at the conclusion that "neither the history of the case nor the hospital records as presented to the department contained any reference whatever to *causes existing prior to landing*, giving rise to the alien's present insanity.

"That the statement that the alien's insanity is caused by constitutional psychopathic tendencies or mental instability, or other predisposing causes existing prior to landing, is given in the form of a bald medical opinion or conclusion, unaccompanied by any facts or reasons showing on what it is based.

"That there is not an affirmative fact in the record, including the family history and the hospital history of the alien, tending to show either that the alien exhibited constitutional psychopathic tendencies and mental instability at the time of landing or prior thereto, or that such constitutional psychopathic tendencies, or mental instability, or other predisposing causes likely to lead to insanity, could by any known means have been detected at that time.

"That in view of this wholly negative aspect of the evidence, it must be assumed that the medical opinion concerning the underlying insanity and the prior existence thereof is wholly *ex post facto*, because the alien has become insane; the alien was a person of constitutional psychopathic tendencies and mental instability; and because the alien was such a person when insanity developed, the alien was such a person at all prior times.

"That in many cases, as in this, some circumstances or event in the life of the alien since landing affirmatively appear from the evidence, suggesting to the ordinary mind an adequate cause to account for present insanity, independently of any constitutional psychopathic tendencies or mental instability on the part of the individual, *e. g.*, as the account in the present case of a sexual assault upon an ignorant sixteen-year-old girl in her own home, and the ensuing shame and worry on her part."

As a matter of fact, there was no record whatever of sexual trauma in this case, and the parents, the relatives, and friends of the alien positively denied that any such occurrence had ever taken place. Here we have the most remarkable position taken by a great department of the Federal Government, in which, from a medical standpoint at least, an uneducated, inexperienced, and entirely incompetent person undertakes to overrule, in a most nonchalant and matter-of-fact manner, the carefully considered opinions of the medical superintendent of a State hospital, a man of national reputation as an alienist; the chief of the Bureau of Deportation, whose experience in examining the mental conditions of aliens is not inconsiderable; a passed assistant surgeon of the Public Health and Marine Hospital Service, a service which claims to number among its members men of no small scientific attainments, and the Commissioner of Immigration at Ellis Island. As a result of this very remarkable position taken by the Attorney-General of the United States, not only was the State of New York compelled to return this insane alien to a State hospital, but it is compelled to maintain her for so long as she may remain insane, which, it is believed, will be for the rest of her life. In addition, this decision was printed by the Department of Commerce and Labor and spread broadcast among the steamship companies and immigration officials, and used as a basis for the cancellation of a great number of warrants issued by the New York State authorities. In fact, the department seems to lose no opportunity for treating with open contempt the medical opinions presented to it.

That I may not seem to be speaking without warrant of fact, let me give an example (and here I quote from the report of Doctor Campbell, of the Bureau of Deportation, mentioned before).

"A case of dementia præcox of the paranoid type was certified to by the medical superintendent of that hospital (Gowanda State) on the grounds of constitutional psychopathic tendencies, mental instability, and deterioration. Upon the recommendation of a lay inspector the Department of Commerce and Labor cancelled the warrant of arrest. Upon a request to the Department of Commerce and Labor by this bureau for an examination by a qualified medical officer of the Public Health and Marine Hospital Service, the following decision of the Commissioner of Immigration was received through the Hon. John H. Clark, under date of October 3, 1912:

“It is noted that Dr. Campbell requests that a properly qualified medical officer of the Public Health and Marine Hospital Service be assigned to reëxamine the above-named alien with a view to her deportation. You are requested to advise Doctor Campbell that such a proceeding is deemed impracticable and unnecessary, as it is considered that this case has received the most careful attention, and the facts relating thereto were thoroughly investigated before arriving at a decision. The matter is therefore closed so far as the bureau is concerned.’”

In case, however, that the State authorities are fortunate enough to have surmounted these various stringent rules, they must still bear the expense of maintenance of the alien for a considerable period, as provided for in this Subdivision 3 of Rule 22 of the Department of Commerce and Labor:

“The cost of maintaining aliens during these proceedings may be borne by the Government, but as to aliens who have become public charges from causes existing prior to landing, such cost will be allowed only for the period subsequent to the date of issuance of warrant of arrest, and then only in case this is followed by an order of deportation. Maintenance bills under this rule shall be delivered to the immigration officer in immediate charge of the case within twenty days from the close of the calendar month in which occurs the death of the alien or removal from the institution for deportation, and failure so to render them shall relieve the United States from any responsibility for the payment thereof. If proceedings against a procurer or contractor are instituted (Sections 3, 5, or 20), immigration officers shall report to the United States District Attorney the amount of the cost of deporting the alien, including one-half of the entire cost of removal to the port of deportation, so that a proper effort may be made to recover such expense from the procurer or importer and the reimbursement of the Government and the transportation company for their respective parts thereof.”

When deportation was first undertaken the State was reimbursed from the day of the admission of the alien into the State hospital, which, it would seem, was a most just proceeding if the alien was improperly in the State of New York. This custom, however, was soon modified, and the State was reimbursed from the time that the Department of Commerce and Labor was notified that a deportable alien was in the hospital. Still another modification was later made, and the State was reimbursed from the time the State authorities were able to verify the landing of the alien in this country. As we have seen, it is now so arranged that the State is reimbursed only from the time that the warrant of arrest is issued, a matter of sometimes but a few days, while the time elapsing from the notification to the Federal Government by the Bureau of Deportation of the presence of an insane alien

in this State may be several months. And yet even though this alien be subsequently deported under Federal warrant, the State of New York must continue to maintain him instead of the Federal Government.² Under the first method of procedure mentioned the moneys received from the United States Government for the reimbursement of this State more than paid the expenses of the Bureau of Deportation, but now the amount so received is but a trifle.

Before further considering the subject of deportation, it may be wise to take up the general proposition as to the whole number of insane in the State, the number of foreign born and the number of native born, the number of aliens, and the relation which the latter bear to the former, as well as to the methods employed, both at the ports of emigration and immigration, to prevent the entry of mental defectives into the United States.

The statistics which are now presented are based upon figures obtained from the New York State Hospital Commission, and not upon data collected by this Commission. This statement is made for the reason that in the report which will be submitted at a later date, the figures which will be given will not correspond exactly with those which are given here, for the reason that the statistics gathered by the State Hospital Commission were not especially directed toward the question under discussion, but had for their main proposition the nativity rather than citizenship, while the statistics which this Commission is now gathering, and which will be explained farther on in this paper, are based upon both nativity and citizenship. It might be further added that the estimates as to cost of maintenance and as to actual numbers of aliens in the tables in this paper are smaller than the figures which will be submitted in the future report.

In February, 1912, there were in the State Hospitals for the Insane 32,662 patients. Of these, 17,853 were native born and 13,163 were foreign born, or, roughly speaking, 45 per cent. were of foreign birth. Of these a large proportion were aliens, but the exact number it is impossible to state.

"In 1900³ the foreign born constituted 26 per cent. of the total population of the State, and in 1910, 29.9 per cent." (These are census periods.) "The foreign-born population of the State therefore contributes relatively a larger number of patients to the State Hospitals than the native population. The ratio of relative contribution to the civil hospitals in 1903 was 2.44 to 1, and 1912, 1.69 to 1. As children below the age of fifteen years rarely become

² See Rule 22 of Department of Commerce and Labor, Bureau of Immigration and Naturalization, November 15, 1911, third edition.

³ See A Statistical Study of the Foreign-born Insane in the New York State Hospitals, by Horatio M. Pollock, Statistician, State Hospital Commission, New York State Hospital Bulletin April, 1912, p. 10.

insane, a part of the relatively large contribution of foreign-born patients to the State hospitals is due to the fact that the immigrants, when they come to this country are largely between the ages of fifteen and forty years, and therefore contain a relatively larger number of adults than the native population. As an offset, however, to the relatively greater number of adults among the foreign born is the relatively greater number of persons of advanced age among the native born. No statistics of the age distribution of the population of the State at the time of the 1910 census are available. It is therefore impossible to calculate just what allowance should be made in determining the relative frequency of insanity among the foreign born.

"The study made by the Federal Census Bureau in 1914 showed that the relative frequency of insanity among the foreign born in the various States differed in accordance with the nationalities composing the foreign-born population. Taking the country as a whole, however, the foreign born, which in 1900 formed only 19.5 of the total population of ten years of age and over, contributed 34.3 per cent. of the insane. A closer comparison of the relative frequency of insanity among nationalities will be found in the analysis of first admissions for New York City.

"The nationality of the insane population in the State varies as the tide of immigration shifts from one section of Europe to another. Until recent years the greater part of the immigrants settling in New York State came from Ireland and Germany. During the past decade these people have practically ceased to immigrate, but instead large numbers have come to the State from Austria-Hungary, Russia, and Italy."

Doctor Pollock says that relatively there has been a decrease in the insane population from Ireland, Germany, England, and Wales, and an increase in the insane population from Russia and Poland, Italy, and Hungary and Bohemia. (See Chart I.) The Census Bureau's report of 1904 did not give separately the number of patients born in Austria. This country now contributes 4.5 per cent. of the population of the civil hospitals and 5.3 per cent. of the population of the hospitals for the criminal insane.

On Chart II, which relates to the increase of native-born and the increase in foreign-born insane in New York State as compared with the general population, in their respective classes, the most striking fact is that during the period from 1900 to 1910 (which years are taken as a basis because they are census periods) the increase in the native-born population was 18.4 per cent. as against 44.4 for the foreign, and yet the increase in native-born patients in the civil State hospitals was 35.7 per cent. while the foreign born was 18.5. On the face of it this would indicate that the insanity rate among the foreign born was decreasing as compared with the native born; but if we go a little farther we will see that

during practically this same period, or from 1903 to 1912 (which dates are taken because they approximate the census dates and are the only figures at present available), the State authorities, through the Bureau of Deportation, deported and repatriated or

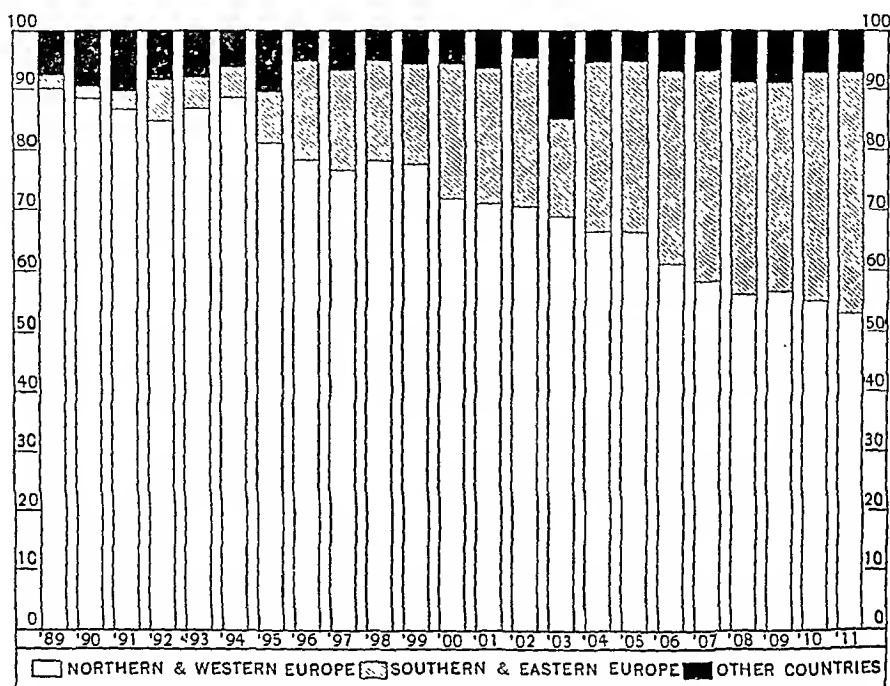


CHART I.—Percentage of patients born in different sections of Europe admitted annually to the New York State hospitals, 1889 to 1911.

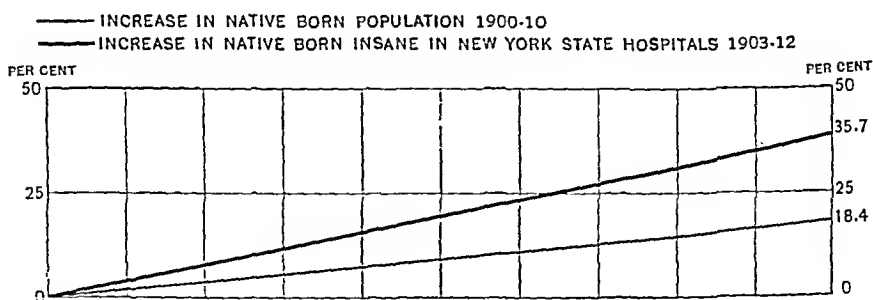


CHART II.—Increase of native-born population compared with increase of native-born insane in New York State hospitals, 1903 to 1912.

returned to their homes, 4,648 patients. And of these the probable number who would have remained in the State hospitals on May 12, 1912, is 3350, making the total of foreign born 16,695, or an increase since 1903, of 48.3 per cent. in the foreign born as against 35.6 per cent. native born.

Memoranda to accompany charts relative to increase of native-born and increase of foreign-born insane in New York State compared with the general population in the respective classes.

NATIVE WHITE POPULATION OF NEW YORK STATE.

	Number.	Per cent. of total.
1900	5,267,358	72.5
1910	6,237,661	68.4
Increase, 18.4 per cent.		

FOREIGN WHITE POPULATION OF NEW YORK STATE.

	Number.	Per cent. of total.
1900	1,889,523	26.0
1910	2,729,260	29.9
Increase, 44.4 per cent.		

PATIENT POPULATION OF CIVIL STATE HOSPITALS.

	Native born.		Foreign born.	
	Number.	Per cent.	Number.	Per cent.
December 31, 1903	13,110	53.1	11,258	46.9
May 6, 1912	17,792	56.4	13,345	42.3
Per cent. of increase	35.7	18.5

Number of foreign-born insane deported and returned to their homes from 1903 to May 1912, 4648.

Probable number of these who would have remained in the State hospitals, May, 1912, 3350, making the foreign-born total 16,695 and the increase since 1903, 48.3 per cent.

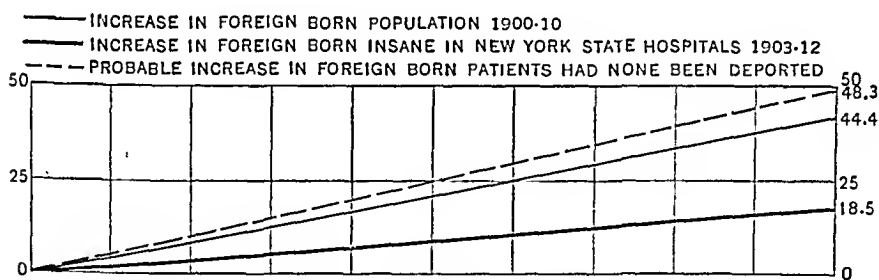


CHART III.—Increase in foreign-born population compared with increase in foreign-born insane in New York State hospitals, 1903 to 1912.

In computing the number that would have remained in the State hospitals at the time of the census of May 6, 1912, it is assumed that the average complete hospital life of a foreign-born patient is eleven years, and that the number of those deported who would have left the hospitals before the time of taking the census bears the same relation to the whole number deported during the year, as the number of years elapsed since deportation bears to eleven. In other words, it is assumed that an equal number of discharges is made during each year. While the result obtained by this method is only an approximation, it may fairly be considered as indicative

of the probable result. The figures for the different years, with the fraction still remaining, are shown in the following tabulation:

Year.	Total foreign born returned to homes.	Fraction remain- ing May, 1912.	Probable number in hospitals Feb. 10, 1912, had none been returned.
1903-4	201	$\frac{3}{11}$	55
1904-5	334	$\frac{4}{11}$	121
1905-6	336	$\frac{5}{11}$	153
1906-7	403	$\frac{6}{11}$	220
1907-8	476	$\frac{7}{11}$	303
1908-9	539	$\frac{8}{11}$	392
1909-10	689	$\frac{9}{11}$	562
1910-11	887	$\frac{10}{11}$	801
1911-12, app.	785	$\frac{12.5}{13.2}$	743
	4648		3350

These figures are not quite correct, as they are not based upon absolutely accurate data, but the number of aliens in the corrected tables will be found to be, we are quite confident, greater than here given.⁴

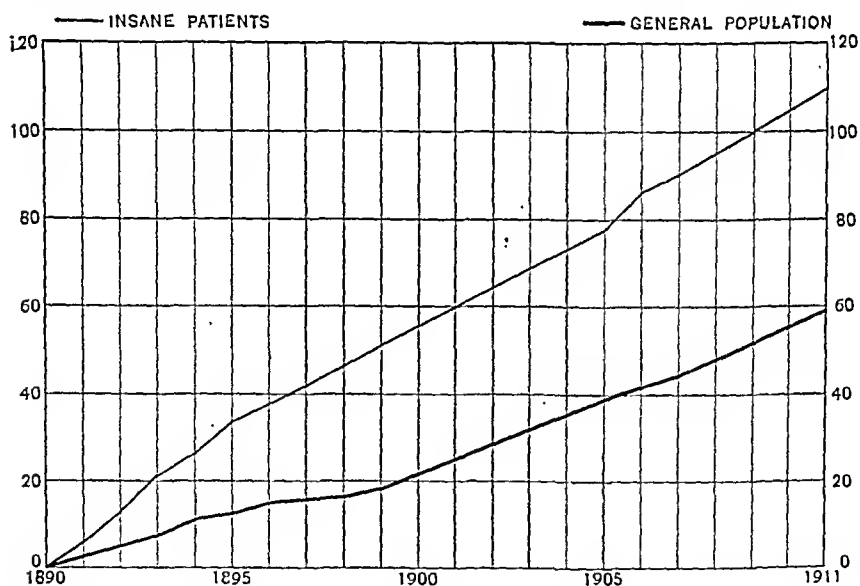


CHART IV.—Increase of insane patients in all institutions in New York State, compared with increase of population, 1890 to 1911.

It is estimated by the statistician of the New York State Hospital Commission, Doctor Horatio M. Pollock, that the cost of maintenance per annum for patients in the State hospitals averages \$262 per year, and that the total cost of maintaining an average patient is \$2282; so that the estimated cost to the State of New York

⁴ Chart IV gives a graphic illustration of the increase in the insane population of State institutions compared with the increase of general population, 1890 to 1911.

(excluding the hospitals for the criminal insane and King's Park and Binghamton, which latter collectively have a population of 5800, but for which no figures are now available) for the aliens in the State hospitals on September 30, 1911, if they live out their expectancy, would be approximately \$10,000,000, and this refers only to the aliens *now* in the hospitals.

Recognizing the serious economic factor to the State, the Legislature, at the suggestion of former Governor Benjamin B. Odell, Jr., created in 1904, what was then called the State Board of Alienists, and what the last Legislature (1912), with the approval of Governor Dix, has called more properly the Bureau of Deportation.

Chart V shows the number of aliens deported from September 30, 1903, to September 30, 1912, by years, as well as the economic saving effected each year. During the first year of the bureau's existence it will be noted that 176 aliens were deported; that there has been a *gradual* rise in the number deported (and when the word "deported" is used repatriation is also included) each year up to and including the years 1910 and 1911, and that during the period of 1911 and 1912 there is an increase of almost 400, and that the total economic saving to the State during that period by this department of the State Hospital Commission has been \$10,590,925. These figures as to cost are arrived at in the following way:

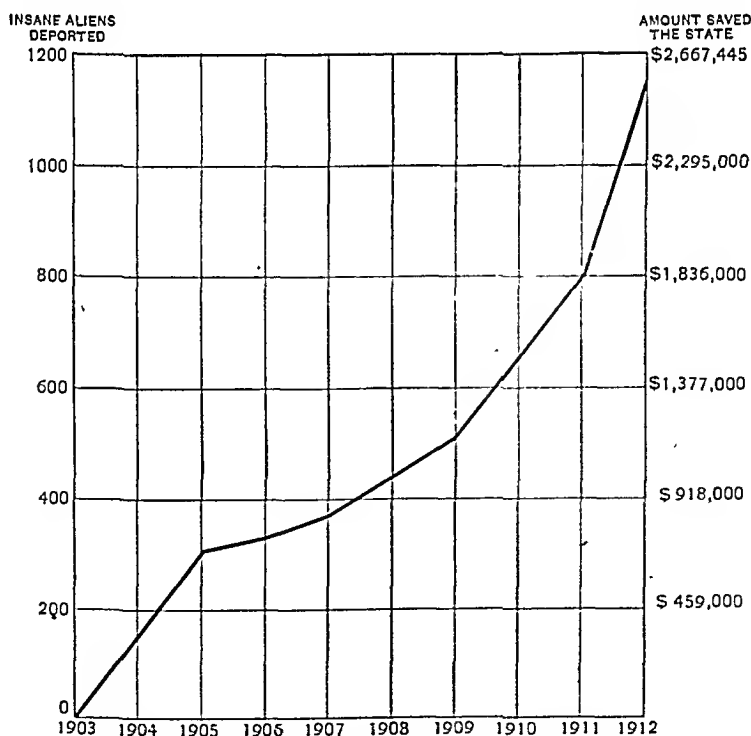


CHART V.—Insane aliens deported by State Hospital Commission with economic savings effected, 1903 to 1912.

Memoranda to accompany chart relative to insane aliens deported by the State Hospital Commission with economic saving effected 1903-12.

The annual cost of maintaining a patient in a New York State hospital averages \$262 per year. This amount is made up of three elements, as follows:

Hospital care, including food, clothes and treatment	\$188
Investment charge, including interest on cost of building and depreciation	70
General supervision, including the expense of the State Hospital Commission, the Bureau of Deportation, and the Psychiatric Institute	4

The average hospital life of a patient is approximately eleven years. The total cost of maintaining the average patient is \$2882. In case a patient is deported soon after admission the saving to the State would be the present worth of \$262 expended annually for eleven years. This is found to be \$2295. Therefore the economic saving resulting from deportations of alien insane each year, since the beginning of the fiscal year of 1903, is as follows:

Year.	Alien deportation.	Economic saving effected.
1903-4	176 × \$2295	\$403,920
1904-5	299 × 2295	686,205
1905-6	307 × 2295	704,565
1906-7	352 × 2295	807,840
1907-8	424 × 2295	973,080
1908-9	489 × 2295	1,122,255
1909-10	613 × 2295	1,406,835
1910-11	784 × 2295	1,799,280
1911-12	1171 × 2295	2,687,445
		<hr/> \$10,590,925

Later on in this paper the methods employed for deportation and repatriation, as well as the difficulties encountered by the Bureau of Deportation, will be considered.

The total estimated capacity of the civil State Hospitals for the Insane on September 30, 1911, as certified by the various hospital superintendents, was 21,276. The total population on that date, we will see, was, without including the hospitals for the criminal insane or King's Park and Binghamton, 25,643. The overcrowding on the particular date was 4367. The number of aliens on that date was 4461. If we deduct from the total population the number of aliens, instead of being overcrowded 4367, it can be readily seen we will have room and to spare for several years to come for our native-born insane. An example of this overcrowding may be seen if we take the figures of one hospital:

MANHATTAN STATE HOSPITAL.

Capacity	3596
Population	4702
Overcrowded	<hr/> 1106
Aliens	1905

It must be remembered that there are two hospitals for the insane criminals, the figures for which are not here included. It is unfortunate that we are unable to give more accurate figures, but we have been unable as yet to obtain full data as to Binghamton and King's Park.

A more interesting factor than the question of cost of maintenance, a more serious phase of the problem than the mere question of money, the question of heredity, will be seen by reference to Chart VI, which is based upon nativity and parentage of first admissions to the State hospitals for the year ending September 30, 1911.

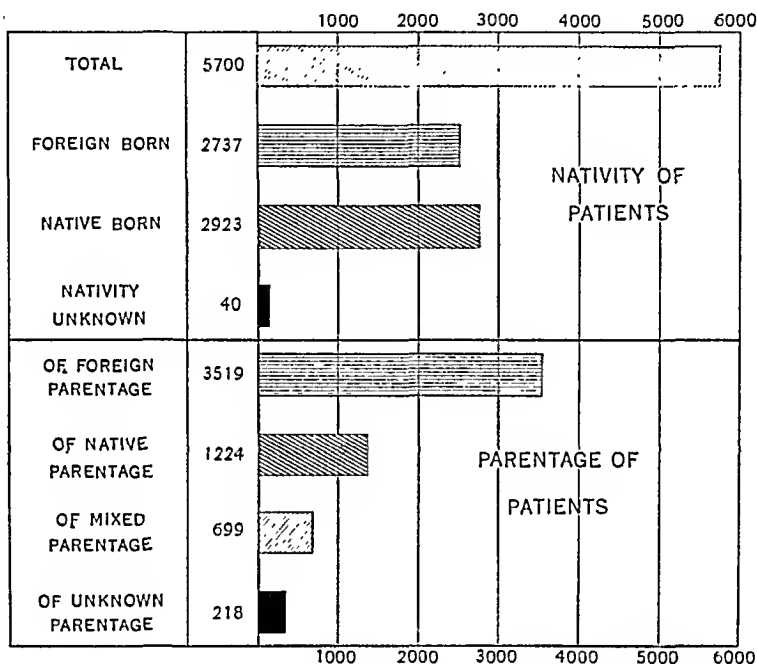


CHART VI.—Nativity and parentage of first admissions to the State hospitals, year ending September 30, 1911.

Memoranda to accompany chart on nativity and parentage of first admissions to the State hospitals for the year ending September 30, 1911.

Total first admissions to the State hospitals, 5700. Of these 2737 were foreign born, 2923 native born, and 40 of unknown nativity.

The foreign born first admissions constitute 48.36 per cent. of the total number of those whose birthplace was ascertained.

The parents of 3519 of the 5700 first admissions were foreign born and of 1224 native born. 699 first admissions had mixed parentage, *i. e.*, one parent was native born and the other foreign born, or one parent unknown and the other either native born or

foreign born. The parentage of 218 of the patients was unknown. The patients whose parents were of either foreign or mixed parentage constituted 74 per cent. of the whole. If only the patients whose parentage was ascertained were considered, those having foreign and mixed parentage constitute 76.9 per cent. of the whole. The first admissions with both parents of foreign birth constitute 64.2 per cent. of the patients the nativity of whose parents was ascertained.

The most prevalent psychosis is a matter of some interest to us, from both the eugenic and the financial standpoint. As testified

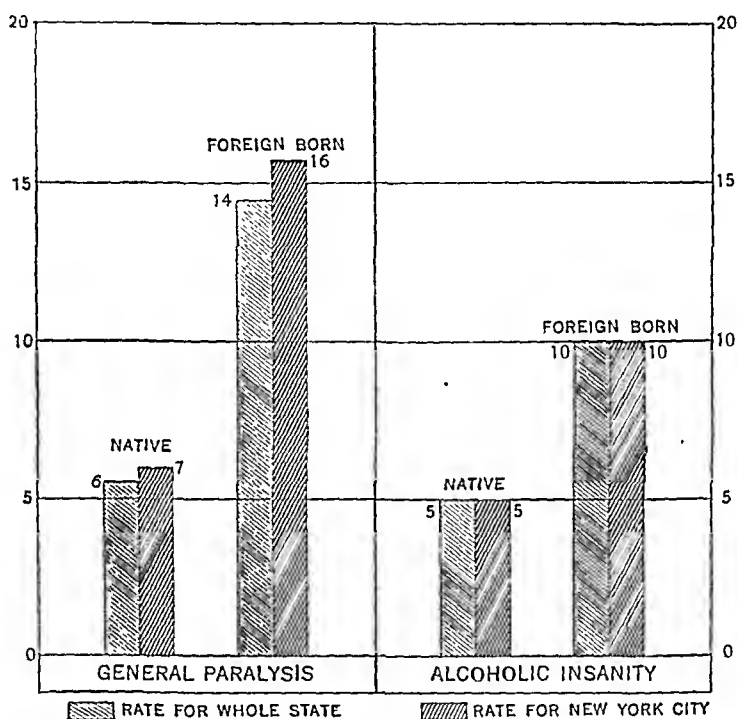


CHART VII.—Rate of frequency of general paralysis and alcoholic insanity per 100,000 of population, first admissions, 1911.

to by the various hospital superintendents, and by reference to the statistics of the State Hospital Commission, we are informed that the most prevalent psychosis is what is now generally known as dementia præcox, the second general paresis, and the third alcoholic dementia. Chart VII gives an illustration of the relative frequency of general paresis and alcoholic insanity among the native born and foreign born. There is no chart to show the relative frequency between the native born and foreign born as to dementia præcox, the testimony of the hospital superintendents indicating that the difference is immaterial. It will be seen here that there is a far larger rate of general paresis and alco-

holic insanity among the foreign born than among the native born when we consider the greater native-born population. There is an additional factor here which should attract our attention, and that is that a large proportion of the patients admitted to our hospitals of foreign birth are young adults, most of them in an otherwise healthy condition, while the admissions for the native born cover all ages up to and including very old age. In these three psychoses it is no uncommon occurrence for a patient to have a lucid interval of a considerable length, during which time he is discharged from the hospital, and many of these patients marry and have offspring to whom, of course, is transmitted an hereditary taint, which may, in a considerable measure, account for the fact that the percentage of those having both parents of foreign birth is considerably greater than those having both parents native born.

Memoranda to accompany chart relative to frequency of general paresis and alcoholic insanity among the native born and foreign born.

General paresis and alcoholic insanity are of special significance on account of their being due to faulty methods of living. Among the 5700 first admissions to the State hospitals for the year ending September 30, 1911, there were 758 cases of general paresis and 580 cases of alcoholic insanity. Comparing the number of cases with the general population, classified with respect to nativity, we find that in general paresis the native born of the State at large had 6 cases per 100,000 and the foreign born 14 per 100,000. Taking the population of New York City alone, we find that there were 7 cases of general paresis per 100,000 of population among the native born and 16 cases among the foreign born. The rates of alcoholic insanity both of New York City and for the whole State were 5 per 100,000 among the native born and 10 per 100,000 among the foreign born.

An examination of the immigration officials and the representatives of the various steamship companies entering the port of New York throws a clear light upon the reason for this enormous burden of mental incompetents which this State, more than any other State in this country, is obliged to bear. Various methods are employed at various points of embarkation. In some parts of southern Europe stations are maintained which are called "control stations," where the intending immigrant is examined by officials of the country from which they come and by steamship officials to ascertain if they come within the requirements of the Federal law. In addition to this they are examined again in the same manner upon the wharf of the steamship company before embarkation. In England there is but this one examination, which is conducted upon the wharf of the steamship company or upon a lighter which carries the immigrant to the ship. In Italy the examination is made at the various ports by an official

of the Italian Government, in some instances assisted by (through the courtesy of the Italian Government) an officer of the United States Public Health and Marine Hospital Service. The value of this examination as to the detection of mental incapacities or psychoses may be readily seen when we are told that the immigrants from southern Europe are examined frequently at the rate of about 600 per hour, or 10 per minute; that the English immigrants are examined during the time required for the barge to go from the landing-place to the ship, which means that from 200 to 600 are examined in about half an hour, or from 7 to 21 per minute; and at the Italian ports (where it is claimed the examinations are the most thorough of any of those made at the ports of emigration) the lowest rate given is 200 per hour and the highest rate 400 per hour, or about 3 to 6 per minute. We are further told that these patients are under observation during their journey from the port of emigration to Ellis Island, but that no special examination is made as to their mental condition. As to what happens at Ellis Island, let me quote from an address of the Hon. William Williams, United States Commissioner of Immigration, before the Mental Hygiene Conference at New York City, November 14, 1912, in which address he says:

"I shall refer only to the detection of the mental diseases with which immigrants may be afflicted, and shall show how inadequate are the ways and means which Congress has provided therefor. I am one of those who believe that the Legislature does only half its duty when it enacts a good law. The other half is to furnish adequate machinery and ways and means for its execution, without which the law accomplishes only a part of its purpose, and is there to perplex executive officials whose sworn duty and desire it is to execute it.

"Immigration to this country is at a very heavy rate. In round numbers it has, during each of the past ten years, averaged 900,000 annually, and the great bulk of it has been through Ellis Island. Only last month there arrived at New York over 80,000 aliens, an average of nearly 2600 a day. Nor are the arrivals evenly distributed over the days of the months, on the contrary there arrive, sometimes for several days in succession, 4000 or 5000 a day. A great many of these people come from the poorer classes of the poorer countries of Europe. Their general physical condition is often far from good and their ignorance beyond belief. Not only are many illiterate, but many do not know the days of the week, the months of the year, their ages, or any country in Europe outside of their own. These people speak many strange tongues and dialects, and interpreters familiar with approximately forty are necessary to enable the Government authorities to converse with them. A number of those who are undesirable additions to our population are nevertheless admissible under the low requirements of existing law. Obviously the task of picking out from among

this heterogeneous mass those suffering from any mental disability is a gigantic one. It would be impossible of complete performance even if the medical staff were in size what it should be. But Ellis Island has to transact its heavy business with the instrumentalities and facilities which Congress provides. It has in all 650 officials. Of these about 130 belong to the Public Health Service, which number includes all medical officers (doctors), hospital attendants, and nurses. The medical officers number only 21, far too few, for they have to perform a multitude of duties in relation both to the inspection of the masses of immigrants who arrive and the care of those detained in the Ellis Island hospitals for sickness, such sick numbering at times several hundred.

"The process of medical inspection is roughly this: Each immigrant passes before two medical officers who rapidly look him over with a trained eye and set aside for special examination all who bear any indications of physical or mental defects. Those so set aside are, for the purposes of mental examination, subjected to well systematized test questions, which the medical officers have evolved from their own special experience, and they apply also such recent modern and scientific methods as those worked out by Binet-Simon, Fernald, Goddard, and others. All such special cases, of which last year there were about 5000, are gone into very thoroughly and are often detained eight days, or longer, for mental observation. But not enough cases are thus set aside, because the medical officers are compelled to work too quickly and lack the requisite number of interpreters to enable them to converse with each immigrant as he goes by. Furthermore, the space at Ellis Island available for the observation of immigrants suspected to be suffering from mental defects is too small."

And he further states that he has frequently called attention, to these matters, asking for an additional force of inspectors, for better accommodations for the examination of the incoming immigrants, and for various other necessary matters, and that Congress has, to a limited extent only, taken note of these matters. And I should like to say just here that if the Federal Government, as constituted by Congress, were as heartily in accord with providing means for the detection of mental defectives as the authorities at Ellis Island are in the execution of the laws, a large measure of our problem would have been long since solved.

There are two methods by which aliens are returned to their native country. One I have already described to you in an earlier part of this paper as deportation, in which all expenses are borne by the steamship companies. The other is the method which is known as repatriation, and the most remarkable condition connected with the problem of the alien insane confronts us here. The State of New York repatriates annually many more aliens than are deported by Federal warrant, *and yet they are repatriated only upon their own consent and through the courtesy of the various steamship*

companies entering the port of New York, and through no right of the State whatsoever. Further, they are repatriated entirely at the expense of the State of New York, which first ascertains the willingness of the alien to return, next whether his friends in the country from which he emigrated will provide for him when he is returned; further, that he is in a fit condition to travel; and beyond all this, it is the custom not only to buy his ticket to his own home, but to send with him a nurse or attendant whose expenses are paid by the State of New York, and he is still further provided with a sum of money to place in his pocket on his return home. Thus we see that in order to get rid of the undesirable alien, the State of New York must not only obtain his consent and the consent of the steamship company to return him, but must pay a considerable sum of money for that return.

At present the arrangement with the various transportation companies entered into by the Bureau of Deportation, bearing date November 17, 1912, provides that the various steamship companies entering into this agreement will repatriate such patients as are presented to them by the Bureau of Deportation, as represented by Doctor Campbell, who are in a fit condition to travel, who will return voluntarily, and whose relatives and friends will provide for him on his return to his native land.

Various methods have been suggested as a solution of this vexing problem. The one advanced by the steamship officials is that there should be stationed at the ports of emigration United States officials, who should partake in the examination of the intending immigrant, and who would therefore share the responsibility with the officials of the steamship companies and the foreign government, a remedy which obviously would be a most advantageous one to the steamship companies. Another is that there should be stationed upon each ship bearing immigrants to this country United States officials, either physicians or nurses, or both, who should observe the patients from time to time and segregate those apparently suffering from psychoses. Another is that a larger number of inspectors should be provided for at Ellis Island, and that these inspectors should be men trained in the detection of mental incapacities. Another is the providing for a detention hospital in which suspected cases could be isolated for a longer or shorter period until proper observation could be had as to their mental condition. Still another is that the time during which deportation could be had under Federal warrant should be lengthened to five years, to correspond with the time required to become a citizen. It was suggested, as well, that Decision No. 120 should be rescinded and the testimony of competent alienists as to the mental condition be taken as sufficient authority for the issuance of a Federal warrant, if other conditions admit. Another is that the law, instead of providing that the Federal authorities shall show that the causes for the patient's psychosis existed prior to his landing, should provide

that the alien should show that the causes for his psychosis did not occur subsequent to his landing, putting the burden of proof upon the alien rather than upon the Government. The last, and what seems to be, in the general opinion, the most generally approved suggestion, is that the steamship companies shall be made responsible for the mental condition of the immigrant as they are made responsible for his physical condition—that is, that for each alien brought to this country who develops a psychosis within the five-year period, the steamship companies shall be fined \$100 and compelled to return the immigrant to the port from whence he sailed, just as they are to-day fined and penalized in cases of favus and trachoma which they bring to this country.

This commission, known as the Commission to Investigate the Alien Insane, was appointed by the Hon. John A. Dix, Governor of the State of New York, on March 16, 1912, and the information given in this paper was obtained through public hearings held at the various State hospitals throughout the State and at public hearings in the city of New York, at which there have been already taken more than a thousand pages of typewritten testimony. It has been the good fortune of this commission to be able to interest many other States in the same matter, and it has devised two sets of history cards for each patient in the State hospitals, the results of which are now being tabulated, one based upon nativity and the other upon citizenship; and a number of States which have the same problem, only in a lesser degree, have, at the request of this commission, undertaken the collection of identical statistics with those which are being collected in this State. The system which, at the request of this commission, the State Hospital Commission has adopted, and which has been concurred in by the other States which have joined the State of New York in the investigation, is as follows: For each patient in the hospitals for the care of the insane in this State there is a history card, based upon both nativity and citizenship, as will be seen by an examination of the card.

Nativity and Citizenship

.....State Hospital

First Admission

Male

Name	Identification No.
Nativity (county of birth) of patient	
Nativity (county of birth) of father	
Nativity (county of birth) of mother	
Citizenship of patient	American Foreign
If naturalized, how?	By final papers By naturalization of parents
Citizenship of father	American Foreign
If naturalized, how?	By final papers By naturalization of parents
Was father a citizen at time of birth of patient?	
Time of patient in U. S. before admission	Years Months
Total time of patient in State hospitals for insane	Years Months
Date of admission	19

First admission cards are printed on white card-board and readmission on salmon, male with black ink and female with red. And of course the female card differs from the male card in regard to the naturalization questions. In the case of readmissions another card is made similar to the first card, so that first admissions are always kept distinct from readmissions and there is no reduplication. In the investigations of this commission it was found that various interpretations had been placed upon questions asked of different hospital superintendents, and it was thought wise to issue with the history card a circular of information which should define carefully every question asked. This circular of information reads thus:

STATE OF NEW YORK—STATE HOSPITAL COMMISSION.

EXPLANATIONS AND INSTRUCTIONS RELATIVE TO NATIVITY AND CITIZENSHIP CARDS.

The nativity and citizenship cards are to be filled out for all patients (exclusive of transfers) admitted to the State hospitals each year from 1905 to 1912 inclusive.

First admissions should be kept separate from readmissions and males from females. The cards of each year should also be kept separate from those of other years.

First admission cards are printed on white card-board and readmission on salmon, male with black ink and female with red.

The name of the patient should be given in full.

- * In reporting the nativity the United States census classification of countries should be used as a guide. If in any case the country of birth can not be ascertained, state whether person is foreign or native born.

The citizenship of the patient and of the father of the patient should be definitely reported as American or foreign. Foreign-born persons are considered aliens unless naturalized, and their citizenship should be reported as foreign *if evidence of their naturalization cannot be produced.*⁶

Aliens may be naturalized in several ways, as follows:

1. By making required declarations and receiving final naturalization papers from a court of competent jurisdiction.

2. A woman by the naturalization of her husband or by marriage to a citizen.

3. Minors by the naturalization of their parents.

A child born in the United States is a citizen regardless of parentage.

A woman loses her citizenship by marriage to a foreigner.

A declaration of intention does not confer rights of citizenship; a foreigner is an alien until actually naturalized. An alien, to be eligible for citizenship, must have resided in the United States continuously for five years.

The time spent in the United States before admission or readmission should be given definitely in years and months. The time spent by the patient in State hospitals for the insane should include all admissions, and, in case patient is still in hospital, should be reckoned to September 30, 1912.

Cards, when filled out, should be forwarded to the State Hospital Commission.

Among the States which have undertaken a similar inquiry are the following: New Hampshire, Connecticut, Massachusetts, Rhode Island, New Jersey, Pennsylvania, Maryland, Indiana, Illinois, West Virginia, South Carolina. Heretofore there has been a lack of uniformity in statistics relating to the insane and I know of none published relating to citizenship, both of which wants are supplied by the adoption of these cards by these various States. It is the intention of this commission, when the full and complete data is collected, to call a public meeting in the city of New York of the representatives of these various States and of other individuals and organizations interested in the matter, to discuss ways and means for a solution of this problem.

⁶ A foreign-born person whose parents are citizens of the United States is not an alien.

COMBINED TUBERCULOSIS AND CARCINOMA OF THE STOMACH, WITH A REPORT OF A CASE UPON WHICH A PARTIAL GASTRECTOMY WAS PERFORMED.¹

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THE present consensus of opinion regarding the coexistence of tuberculous inflammation and cancer coincides with that put forward by Bayle in 1810. Cancer and tuberculosis can occur in the same individual and in the same organ.

In 1830 Rokitansky claimed there was a mutual antagonism between cancer and tuberculosis. This doctrine was assailed by the French school under Lebert (1844-51). Experience has proved Lebert's views to have been correct. With the gradual accumulation of pathologic facts we know there is no specific antagonism between cancer and tuberculosis, and that cancer and tuberculosis can occur in the same individual and in the same organ.

A great deal of careful work has been done upon this subject, and the academic discussion that has centred around the question has produced an extensive literature. In Germany some of the more modern articles of worth are those by Lubarsch, Borst, Zenker, Ribbert, Naegeli, Baumgarten, Barchasch, Ehrler, Tauschwitz; in France we have the classic monograph of Claude; in America the articles of Pepper and Edsall, Crowder, Warthin, Moak, Bastedo, Stettin, and Oertel. Bastedo deals with the association of cancer and tuberculosis in general, and gives a summary of the literature. Stettin ably deals with the coexistence of tuberculosis and carcinoma in the intestine. Oertel discusses the relative local influence of coexisting tuberculous inflammation and cancer; he emphasizes the fact that enlarged glands in the neighborhood of a malignant tumor may be tubercular and show no evidence of malignancy. This fact must be kept in mind in weighing the clinical value of enlarged glands in the determination of malignancy (see Table B).

The combination of tuberculosis and carcinoma of the stomach is rare. Case No. 1 was discovered by operation, the remaining cases by autopsy.

The interesting point in this case, beside the association of these two supposedly antagonistic lesions, is the sequence of the lesions.

¹ The case was shown before the Surgical Section of the Academy of Medicine, 1907. The pathologic specimen was demonstrated before the Society of Clinical Surgery, 1907, by Prof. F. C. Wood.

From the clinical and pathologic evidence it seems probable that the original lesion of the stomach was a tuberculous ulcer of the pylorus, secondary to possible old lesion of the right apex. From this tuberculous ulcer a diffuse carcinoma developed.

The following is a summary of the reported cases of combined tuberculosis and cancer of the stomach, and includes a personal case upon which a partial gastrectomy was performed:

TABLE A.—COMBINED TUBERCULOSIS AND CARCINOMA OF STOMACH.

CASE I.—Lyle, H. H. M. (1907). Combined tuberculosis and carcinoma of the stomach; partial gastrectomy; death two years and two months later. Patient, aged forty years. Irish, porter by occupation, admitted May 2, 1907; discharged cured, May 30, 1907.

History: One brother and sister died of pulmonary tuberculosis. Patient had lues sixteen years ago; treatment for two years. Gonorrhea four times. Operated on for fistula in ano four years ago. Drank ten to fifteen whiskies a day; smoked to excess. Has had a "stomach cough" for a year or more. Five months ago he complained of a dull pain in the region of the stomach; this was accompanied by a moderate amount of gaseous distention; the pains and distention have gradually increased. The patient started vomiting four months ago, and this has persisted. The vomiting took place three to four hours after eating; the vomitus was large in amount, and consisted of the contents of the stomach and undigested food; at times it contained food that had been eaten three or four days previously; has vomited coffee-ground material. Constipation marked; bowels have not moved for seven days. Has lost thirty pounds in three months, and has rapidly grown weaker.

Physical Examination: Man, medium frame, emaciated; weight, one hundred pounds. Skin and mucous membranes anemic; superficial glands enlarged. Possible old tuberculous lesion at right apex. Abdomen: Flat, with visible peristalsis; on deep palpation a hard mass about the size of a walnut was found in the epigastric region to the right of the median line; was movable; moved with respiration, and could be fixed with the hand. Lower border of the stomach, two fingers' breadth below the umbilicus, succussion splash was present. Blood: cells normal; hemoglobin, 70 per cent. Gastric analysis: total acidity, 49; HCl, 20; loosely combined, 13; lactic acid present; starch poorly digested; mucus abundant; no blood; no pus; sarcinæ ventriculi and Boas-Oppler bacilli present. A full evening meal was given. The contents expressed next morning contained partly digested meat and raisins. The raisins had been given four days previously.

Diagnosis: Carcinomatous stricture of pylorus, with dilatation of stomach.

Operation by Dr. Lyle, May 5, 1907. Partial gastrectomy, with gastrojejunostomy, according to Billroth's second method. The portion removed included two inches of the duodenum, the pylorus, and the stomach to the Hartmann-Mikulicz line, with the corresponding glands.

Pathologic Report, by Prof. Francis C. Wood. Diffuse carcinoma of the stomach; tuberculosis of submucosa.

Macroscopic Examination: The specimen consists of a complete section of pylorus, plus a portion of the stomach 8 c.m. in length. At the pyloric end the wall is thickened to 1 cm. by dense tissue, which has a uniform light colored, cut surface. Glands enlarged.

Microscopic Examination: Sections show the mucous membrane in places to be entirely gone; the submucosa is infiltrated, with small round cells. The muscular coats have long rows and small groups of gland cells situated between the muscular fibers. The groups of cells are to a marked degree surrounded and infiltrated with numerous small round cells. We also find two or three areas of coagulation necrosis, one of which contains well-formed giant cells and some epithelial cells.

The patient made an uneventful recovery. There was no shock, and the highest temperature was $100\frac{2}{5}^{\circ}$. He left the hospital May 30, 1907.

Subsequent History: July 2, 1907. Patient has gained forty-five pounds, is working, carrying trunks, etc.; feels well and strong. Eats and digests well. Calmette's ocular test for tuberculosis negative.

September. Has had an attack of diarrhea after partaking of a generous meal of corned beef and cabbage. Attack controlled by the administration of dilute HCl with meals.

February, 1908. Patient continues in good health. Does not react to tuberculin. Has been drinking ten to twelve whiskies a day, without any apparent effect.

March 28. Patient is in good health; no signs of recurrence. Ewald's test meal given. At the end of one hour the stomach was found to be empty. Contents expressed one-half hour after the test-breakfast gave the following results on chemical examination: No free HCl; total acidity, 1.8; no lactic acid; no Boas-Oppler bacilli; no sarcinæ ventriculi; no blood; very little mucus. The patient remained well and continued steadily at work for two years and two months. He was admitted to the tubercular service, with the diagnosis of pulmonary tuberculosis, and developed what was supposed to be an acute intestinal obstruction from adhesions. Under local anesthesia an exploratory laparotomy was performed. On opening the abdomen considerable blood-tinged serum escaped. The intestines were equally distended; no mechanical obstruction

was found. The visceral and parietal peritoneum were studded with numerous small tubercles. The condition was paralytic, not mechanical. The distention was relieved by the formation of a left inguinal colostomy. The operation afforded only temporary relief, as the patient died two days later.

Autopsy, by Dr. Zinsser, July 8, 1909. Body of an emaciated man of middle age. On the abdomen to the right of the midline there is a longitudinal incision, extending 2 cm. below the ensiform to the umbilicus. In the left iliac region there is a fresh colostomy wound. Thorax: on opening the thorax, viscera are found in normal position. The anterior mediastinum is obliterated by adhesions of the pericardium. The pericardial cavity is obliterated by adhesions between the pericardium and the heart. Heart: changes of fatty myocarditis. Lungs: both lungs are adherent throughout their pleural surfaces to the thoracic walls, and are thickly studded with tuberculous foci, which in the lower lobes adhere to the miliary type, becoming thicker and individually larger in the upper lobes. Here areas of phthisical consolidation are seen and a few small cavities are found. The bronchial nodes are enlarged and one or two are cheesy. Abdomen: the peritoneum, both visceral and parietal, is studded with miliary tubercles, which are apparently thicker in distribution in the upper quadrant. Liver and spleen show changes of congestion; pancreas apparently normal. Kidney: changes of parenchymatous nephritis; suprarenals, normal. Stomach: at the site of the old operation there is a hard tumor, about 1 x 2 cm. Intestines show no lesions apart from the miliary tubercles on their serous surfaces. Intestinal walls are extremely friable and much discolored, probably due to postmortem conditions. Bladder, normal.

Anatomic Diagnosis: Pulmonary tuberculosis; miliary tuberculosis of peritoneum and of the intestinal coverings; carcinoma of the stomach; parenchymatous nephritis; and fatty degeneration.

Microscopic Examination: Examination of the scar at the site of the gastric operation shows an infiltration of scar tissue, with carcinomatous cells of a type similar to the original growth. Lungs: typical tuberculosis, both miliary and larger phthisical consolidations. Liver: slightly congested, otherwise normal, except for a few small foci, consisting of acute abscesses, not tuberculous.

CASE II.—Claude (1899). Alveolar epithelioma and tuberculous ulceration of the stomach. Male, aged sixty-one years. Diagnosis: intestinal and pulmonary tuberculosis; no gastric symptoms. Autopsy: tuberculous lesions of large intestine; tuberculous granulations and caseous softenings of both apices; glands of gastrohepatic omentum and along greater curvature enlarged. On the posterior wall of the stomach near the pylorus is an irregular rounded tumor, 6 cm. by 45 mm., pink in color, covered with villous processes. A short distance from this growth

were other small pedunculated growths about the size of peas. The entire portion of the tumor opposite the pylorus was surrounded by a shallow ulceration; 25 mm. of mucous membrane had disappeared from the base of the ulcer.

Microscopic examination shows the growth to be an alveolar epithelioma, with cylindric or polymorphous cells, forming a voluminous tumor, which has been invaded by tuberculosis and in part destroyed by this superadded infection. The small pea-like growths were adenoma. Section through the ulcer showed giant cells, containing tubercle bacilli. Claude was of the opinion that cancer developed on the basis of an adenoma, and that the tuberculosis was superadded.

CASE III.—Simmonds (1900). Carcinoma of the pylorus, with multiple tuberculosis ulcers. Man, aged forty years, died of pulmonary and intestinal tuberculosis. At autopsy a coarse carcinoma the size of a hazel-nut was found, which caused stenosis of the pylorus. The distended stomach contained several small tuberculous ulcers. The observer suggests that the secretory disturbance due to the presence of the carcinoma and diminished production of hydrochloric acid served to favor the growth of the tubercle bacilli in the gastric mucosa.

CASE IV.—Barchasch (1907). Submucous tubercle of the pylorus, with simultaneous carcinoma of the cardia.

Autopsy: the subject, aged forty-five years, presented the following findings, with a simultaneous carcinoma of the cardia orifice; carcinoma of the regional glands; old pulmonary tuberculosis. The rare form of gastric tuberculosis, in the shape of a solitary tubercle, gave no clinical evidence of its presence during life, and was not discovered until autopsy. The interest in this case consists in the combination of tuberculosis and cancer in the stomach. The origin of tuberculosis of the stomach was considered secondary to the pulmonary process, the lack of the HCl favoring the development of the tubercle bacilli.

Microscopic Examination: Adenocarcinoma tuberculosis. Tubercle bacilli were found in the sections of the tubercle. Glands, adenocarcinoma.

CASE V.—Borst. Carcinoma of stomach, with multiple tuberculous ulcers. No clinical details given; case of phthisis, with multiple tuberculous ulcers and carcinoma of the stomach. The stroma of the carcinoma contained tubercle bacilli. Borst considers this a carcinoma invaded by tuberculosis.

CASE VI.—Friedländer. Cancer of the stomach developing on a cicatrix of a round ulcer, which had been invaded by tuberculosis. This case is quoted by Claude (p. 60). I have been unable to verify it.

TABLE B.—ABSTRACT OF CASES WITH CARCINOMA OF THE STOMACH ASSOCIATED WITH TUBERCULOUS LYMPHATIC GLANDS.

Clement (1895). Pyloric carcinoma associated with extensive caseous tuberculosis of the pyloric glands, the glands of the hilum of the liver, and axillary glands.

Metterhauser (1897). Carcinoma of the pylorus, miliary tuberculosis of the liver, and the mesenteric lymph glands.

Naegeli (1897). Carcinoma of the pylorus; caseous tuberculosis of the regional glands.

Lowenstein, quoted by Tauschwitz (p. 17). Have been unable to find original.

Ehrler (1906). Adenocarcinoma of the pylorus, with tuberculosis of retroperitoneal glands. Pylorotomy with gastro-enterostomy, peritoneal infection from leakage, tuberculosis of the rectoperitoneal glands, intestinal tuberculosis, phthisis.

The cases of Archard and Kollech are not included in this table.

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THE CONTROL OF RABIES.¹

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HISTORICAL NOTE. Although reference is made to a disease in dogs, which was no doubt rabies, by Aristotle, as long ago as the fourth century before the Christian era, and distinct epidemics of the disease were recognized as far back as the beginning of the seventeenth century, it was not until about 1875 that it was demonstrated that the disease could be markedly limited in its spread and probably entirely stamped out. Accordingly at about that time several nations adopted rigid regulations for the control of the disease. Such nations have been abundantly rewarded; the disease no longer existing in Great Britain, Norway, Sweden, nor Denmark. With such a remarkable demonstration of the efficacy of a preventive measure it seems indeed strange that most of our civilized nations have not yet adopted measures which if carried out may be relied upon to exterminate the disease. This in face

¹ Read at the Fifteenth International Congress on Hygiene and Demography, Washington, D. C., September, 1912.

of the fact that, taken the world over, the disease is apparently on the increase.

PREVALENCE OF RABIES IN THE WORLD AT THE PRESENT TIME. Rabies is a very widespread disease. With the exception of Australia there is not a continent which is free from it. It is apparently most prevalent in the countries of Europe adjacent to the Mediterranean Sea. On account of the fact that in most countries the disease is not reportable, except as it causes the death of a person, it is impossible to obtain even fairly accurate data as to the number of cases of rabies now in existence. The figures presented in the following table give therefore only an approximate idea as to the number of persons who are annually bitten by rabid or presumably rabid animals:

NUMBER OF PERSONS BITTEN BY RABID OR PRESUMABLY RABID ANIMALS
IN VARIOUS COUNTRIES.

Country.	Number.	Year.	As determined by the number of persons who received the Pasteur antirabic treatment at:
Argentina	417	Average of past twenty-four years	Buenos Aires.
Australia	... ²		
Austria	452	Average of 1907 and 1908	Vienna.
Brazil	583	1911	Sao Paulo.
Bulgaria	1027	1911	
Canada	... ³		
Denmark	0	For past fifty years	
France	467	1909	Paris.
Germany	374	1909	Berlin and Breslau.
Great Britain	0	Since 1902	
Hungary	806	Average 1890 to 1908	Budapest.
Holland	... ⁴	Since 1879, except along the Belgian border	
India	2073	1910	Kasauli.
Italy	3537	1909	Rome, Milan, and Turin.
Philippine Islands	54	Year ending June 30, 1911	Manila.
Portugal	1672	1911	Lisbon.
Russia	3520	1909	St. Petersburg and Charkaw.
Spain	649	1911	Madrid and other places.
Sweden	0	Since 1870	
Switzerland	0	1911	
Turkey	978	1908	
United States	4625	1911	Constantinople.

PREVALENCE OF RABIES IN THE UNITED STATES. In 1900, Salmon⁵ reported that there had been 230 deaths of human beings from rabies in 73 of the principal cities of the United States, from 1890 to 1899.

According to the mortality statistics of the Bureau of the Census the number of deaths of human beings from rabies in the registration area of the United States was 33 in 1900, the number gradually increasing to 85 in 1906, and falling to 75 in 1907.

The Public Health and Marine Hospital Service made an exhaustive study⁶ into the prevalence of the disease in the United States in 1908. According to their findings, rabies was present in

² Never introduced.

³ Never introduced.

⁴ Few cases.

⁵ Salmon, D. E. Year-book, Dept. Agri., 1900.

⁶ Kerr and Stimson. Jour. Amer. Med. Assoc., September 25, 1909, liii, 989.

534 localities distributed throughout the United States, with the exception of 10 States; there occurred 111 deaths of human beings and about 1500 persons received the Pasteur antirabic treatment.

During the past few months I have collected the data relative to the prevalence of the disease in the United States during the year 1911. Data were also collected by the Public Health and Marine Hospital Service.⁷ Such data have been combined in the form of the following table:

States.	Infected localities.		Persons treated in	Disease on increase or decrease—determined by comparing number of cases of the disease in 1911 with those of the previous three years.			Possess State regulation for the control of rabies in dog.
	1908	1911		Increase.	Decrease.	Uncertain.	
Alabama	13	47	281	*			
Arizona	1	1	1		*		*
Arkansas	5	18	29	
California	49	124	*			
Colorado	1	10	10	*			
Connecticut	7	11	8		
Delaware	5	15	22	*			
District of Columbia	1	1	41				
Florida	11	36	128	*			
Georgia	17	4	457	*			
Idaho							
Illinois	18	35	292	*			
Indiana	57	62	104	*			
Iowa	5	29	92	*			
Kansas	4	86	175	*			
Kentucky	7	14	24	*			
Louisiana	3	61	233	*			
Maine							
Maryland	12	59	122	?	
Massachusetts	9	45	27		*		
Michigan	11	46	58	*			
Minnesota	18	31	117		..	?	
Mississippi	10	34	51	..			
Missouri	9	52	187	*			
Montana							
Nebraska	5	?	
Nevada							
New Hampshire	7	3	2	..	*		
New Jersey	41	68	189	*			
New York	52	38	899	..	*	..	*
New Mexico							
North Carolina	19	96	166	*			
North Dakota	2	12	15	*			
Ohio	32	91	275	*			
Oklahoma	6	51	106	*			
Oregon	3	1	..	*		
Pennsylvania	25	52	46	..	*		*
Rhode Island	10	4	5	*		..	
South Carolina	5	32	114	*			
South Dakota	2	7	14	?	
Tennessee	7	16	13	*			
Texas	15	?	
Utah							
Vermont	1	..	0	..	*	..	*
Virginia	37	48	54	?	
Washington	7	2	*			
West Virginia	2	21	30	*			
Wisconsin	42	83	112		..	?	
Wyoming	3	4	*			
Total	534	1381	4625	27	7	7	4

⁷ Stimson, Public Health Reports, July 12, 1912, vol. xxvii, No. 28.

A comparison of the distribution of rabies in the United States in 1908 and 1911 indicates that during the last three years:

1. There has been an increase of rabies in the United States, as indicated by the fact that during 1908 there were 534 infected localities and about 1500 persons received the Pasteur antirabic treatment, whereas in 1911 there were 1381 infected localities and 4625 persons received the treatment.

2. The increase has occurred principally in the Southern and Middle Western States, very few of which have any State regulations concerning the muzzling and movement of dogs.

3. There has been a decrease in the number of cases in most of the New England States, where since the epidemic of rabies several years ago regulations aiming at the control of the disease in dogs have been rather rigidly enforced. In Rhode Island the relaxation in the enforcement of muzzling regulations during the past two years is causing a distinct increase in the number of cases.

4. The disease is somewhat on the increase in the far west, more especially in California. It is believed by some that the spread of rabies in Arizona is due principally to the bite of skunks. With the object of controlling the disease a bounty is being paid for skunks in that State. The secretary of the State Board of Health of Montana informed me that so far as known there has never been a case of rabies within its borders. It would be unfortunate if the disease should gain a foothold among the wild animals of the west, as it has done in some countries.

It is well understood that infection with rabies takes place almost only through a wound, such as the bite of an animal, and that, although any of the warm-blooded animals may be affected, the dog is by far the principal offender.

METHODS WHICH MAY BE EMPLOYED FOR THE CONTROL OR ERADICATION OF RABIES. *Immediate Local Treatment.* The development of the disease can be largely prevented by treatment of the wound with some caustic, preferably nitric acid. Cauterization should, of course, be done as soon as possible after the wound is inflicted. Experiments performed in the research laboratory of the New York City Department of Health indicate that the application of nitric acid is of value even if such application be delayed for twenty-four hours. Dr. Park believes that "in the case of small wounds all the treatment probably indicated will be thorough cauterization with nitric acid within twelve hours from the time of infection."

Pasteur Antirabic Treatment. The Pasteur treatment has largely robbed rabies of its terrors. Previous to 1886, when the treatment was first begun at the Pasteur Institute in Paris, the mortality from rabies of persons bitten by rabid or presumably rabid animals was 16 per cent. (Leblanc). Since that time more

than 30,000 persons have received the preventive treatment at the Paris Institute, with a mortality of only 0.5 of 1 per cent. The Pasteur treatment is given in most of the countries of the globe, and through the Public Health Service is made available in every State of the United States. The results at other institutes have been practically the same as those of the institute at Paris. However efficient this treatment has been in preventing the development of the disease in infected individuals it is probable that the safety assured by the treatment has caused a relaxation in the enforcement of regulations aiming at the control of the disease in dogs and other lower animals. Dr. T. Murillo recently informed me that he believes that for the reason mentioned there are more cases of rabies in Spain at the present time than there were twenty years ago.

Accurate Diagnosis. In practically all countries the clinical diagnosis is confirmed whenever possible by a laboratory examination, consisting of a search for Negri bodies or of an animal inoculation, or both. The mistake that is often made is the killing of the animal so soon as rabies is suspected. If the animals are detained and watched for the development of the disease instead of being killed it will be found that some of the Pasteur treatment which is now being given is unnecessary, but at the present time advisedly administered.

Regulations Aiming at the Control of Rabies in Dogs and Other Lower Animals. Although rabies may be transmitted by the bite of any of the warm-blooded animals the disease is propagated principally by dogs. For that reason regulations aiming at the eradication of the disease, with but occasional exceptions, must be aimed at dogs. The enforcement of the following measures may be relied upon to cause the extermination of rabies:

Licensing. Stray ownerless dogs are the principal offenders, not only in spreading rabies, but in doing harm to live stock. Irrespective of the presence of rabies in a community all dogs ought to be licensed and provided with a collar and license tax and all stray dogs destroyed in a humane manner. The expense of enforcing such a license rule may be maintained by the dog-license fees. The rule has been enforced in England and in the other countries from which rabies has been eradicated. The present decline of the disease in Paris is attributed by Dr. Letulle to the strict enforcement of the regulations regarding the capture of stray dogs.

Muzzling. Wherever rabies is present in a given place all dogs permitted to run at large should be kept muzzled for a period of at least six months after the disappearance of the last case from the locality. There is a difference of opinion as to the size of the territory in which dogs should be muzzled whenever the disease appears. Certainly it should not be less than a city of moderate

size, or in rural communities it should in the United States not be less than an average-sized township. If several cases occur at places several miles apart it is advisable to have the regulations enforced over an area corresponding to a county. If the disease is widespread it is certainly best to have the dogs of an entire State muzzled. The muzzling of dogs is the most important measure in preventing the spread of rabies in a community where the disease exists. In the larger cities of Germany dogs permitted to run at large are always muzzled. The objection to muzzling comes from many well-meaning people who believe that it is cruel. It is not cruel to place a properly constructed (such as the basket type, made of metal) and well-fitting muzzle on a dog. Such a muzzle will permit the dog to open its mouth, pant, and drink, but not to bite. It is no more cruel to put a muzzle on a dog than a bit in a horse's mouth. Of course the dog will resent it at first; so does the horse resent the bit. But once they become accustomed to it they do not mind it. The good effect of this procedure has been demonstrated many times and in many places. Probably the best example is the result brought about in England, as is well shown by the following table:

NUMBER OF CASES OF RABIES IN GREAT BRITAIN.

Year.	Number of cases.	
	Dog.	Human.
1887	217	29
1888	160	14
1889	312	30
Muzzling enforced:		
1890	129	8
1891	79	7
1892	38	6
Opposition to muzzling; ordinance relaxed:		
1893	93	4
1894	248	13
1895	672	20
Muzzling again enforced:		
1896	438	8
1897	151	6
1898	17	2
1899	9	0
1900	6	0
1901	1	0
1902	13	0
1903-07	0	0

Note that with the enforcement of the muzzling law the number of cases of rabies rapidly declined from 217 in 1887 to 38 in 1892. In 1892 the authorities yielded to the petition of "dog lovers" and permitted muzzling to be discontinued. As a result the disease rapidly increased in number, so rapidly that during the third year (1895) 672 dogs and 20 human beings died from rabies. The

muzzling law was again enforced, the number of cases rapidly decreased, and in 1902 entirely disappeared. Since that time no case of rabies has been recognized in Great Britain. Dogs are not muzzled in England at the present time, but we are informed that muzzling will be resumed with the appearance of a single new case of the disease. The existence of a muzzling act should require all dogs not muzzled to be killed by the proper health or police authorities. In some places the right to kill any unmuzzled dog is given to any person. If the law held the owner of a dog legally responsible for all damage done by such, muzzling could be enforced much more readily than is the case at present.

Detention of Dogs. Dogs that have been associated with rabid animals, and are therefore probably infected, should be confined to a kennel or shed for a period of not less than three months, and preferably six months. When taken out for exercise they should be muzzled and led in leash. When the disease is prevalent it is best to have all dogs confined. Females in heat should at no time be permitted to run at large.

Destruction of Dogs. All dogs known to be affected by rabies or to have been bitten by rabid animals should be killed. The mistake that is usually made is to kill an animal immediately after that animal has bitten a person, on the suspicion that it may be affected by rabies. The importance of such an error is realized when we remember that it is not always possible to get laboratory evidence of the disease even when it exists. Whenever possible an animal that has bitten a person should be kept confined for a period of ten days. If the disease does not develop nor the animal die within that time it may be safely concluded that rabies does not exist.

Quarantine. To prevent the introduction of rabies into a country, all dogs that are imported should be held in quarantine for a period of six months. Australia owes to a rigid enforcement of such a law the fact that it has never had a case of rabies. England likewise depends on it to keep the country free from the disease. Such quarantine may likewise be applied to the smaller divisions of a country. During a recent outbreak of the disease in Canada it was prohibited to move dogs from the infested area. In Germany a certificate from an official veterinarian is necessary to have a dog moved from one section to another. The Federal Government might impose a quarantine against a given State should the disease become prevalent within its borders.

There are few diseases that can be so easily eradicated as rabies. We have now the knowledge necessary to secure its disappearance. All that we need is action on the part of our authorities, which to be effectual must of course have the coöperation of the general public. The time is now ripe for organized effort to stamp out

the disease. It has been done in England and can likewise be done in other insular territories. It has been accomplished in Norway, Sweden, and Denmark, and can likewise be done in other peninsular regions. It is more difficult to rid of rabies, inland countries with extensive land boundaries. Even in these much can be accomplished, as has been demonstrated by Germany, Holland, Canada, and some of the eastern States of the United States. It is hardly to be expected, however, that the disease will be entirely eradicated without coöperative or at least simultaneous action on the part of adjoining States or countries. In the United States the question of State rights requires that the efforts be left largely with the individual States. If every State in which the disease exists would take as vigorous steps to exterminate rabies as were taken in England, and if like action were taken by the countries to the south of us, as has substantially already been done by Canada on the north, it would be possible to remove the last vestige of the disease from the North American continent in the course of a few years. In like manner the disease could be eradicated from other continents.

To exterminate rabies it is necessary that the general public should be better informed than it is at present regarding the disease. The people should be made to realize especially:

That rabies is prevalent in most countries the world over, and that in many places—more especially in parts of the United States—it is distinctly on the increase.

That it is possible to exterminate the disease in the course of a few years by the adoption of easily executed regulations concerning dogs.

That in particular the muzzling of dogs is not a hardship to the animal, and that from a sanitary and economic point of view it is advisable to get rid of all stray or ownerless dogs.

That the eradication of rabies is worth while for economic reasons because of the loss to the live-stock industry.

That efforts at its eradication are many times over justified by the loss of human life and the almost endless amount of worry which is now attached to the bite of a dog.

METABOLISM IN PELLAGRA.¹

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INTRODUCTION. A study of the metabolism in pellagra would appear to be of interest from a number of different viewpoints—namely, as an aid to the interpretation of the gastro-intestinal symptoms generally observed; in connection with the maize theory of the etiology of the disease; and, further, because of the resemblance in certain particulars to beriberi,² in which the etiologic factor appears to be an inadequate dietary. Despite the reasons which would seem to make a knowledge of the metabolism in this disease desirable no extended study has been carried out in this connection, with the exception of the work of Camurri,³ in Italy. However, certain points of interest have been noted—namely, the frequent occurrence of gastric anacidity by Johnson,⁴ by Cecconi,⁵ and by Niles,⁶ and the presence of indicanuria by a number of observers, most recently by Ormsby and Singer.⁷

The experiments conducted by Camurri were fairly comprehensive, though directed in particular toward the study of the mineral metabolism. His work included a general study of the composition of the diet, urine, and feces of pellagrins subsisting upon mixed diets and upon diets composed largely of corn. Balances were given for nitrogen, fat, and salt in comparison with

¹ This paper forms a part of the preliminary report of work performed under the auspices of the Thompson-McFadden Pellagra Commission of the Division of Tropical Medicine, Department of Laboratories, New York Post-Graduate Medical School and Hospital. The results of this work were reported at the Second Triennial Meeting of the National Association for the Study of Pellagra, Columbia, S. C., October 3, 1912, and at a meeting of the Section on Medicine of the New York Academy of Medicine, February 18, 1913. The analytical work was carried out with the assistance of Messrs. G. O. Yelovic, W. I. Sivitz, Dr. E. Kister, and Mr. A. Bernhard; and the ward work with the assistance of Mrs. J. H. Brinkerhoff and the Misses H. A. Macarow and H. F. McDowell.

² For discussion of literature on beriberi, see Strong and Crowell, *Philippine Jour. Sci.*, 1912, B, vii, 271.

³ *Atti del Quarto Congresso Pellagrologico Italiano*, Udine, 1910, p. 67.

⁴ *South. Med. Jour.*, 1911, iv, 478.

⁵ *Gazzetta Degli Ospedali e delle Cliniche*, 1911, xxxii, 77.

⁶ *Pellagra*, 1912, p. 77.

⁷ Report of the Pellagra Commission of the State of Illinois, 1911, p. 23; also *Arch. Int. Med.*, 1912, x, 123 and 219.

those of normal individuals upon similar diets. The points of interest will be discussed in connection with our own work.

Johnson found the free hydrochloric acid of the gastric juice to be absent in 14 out of 20 cases, while rennin was absent in 7 cases. Diarrhea was observed in the 14 cases, with absence of free hydrochloric acid, but only in one of the other 6 cases, and here attributed to another cause. Cecconi found free hydrochloric acid absent in all of his 12 cases, while Niles in an examination of 64 cases of undoubted pellagra found free hydrochloric acid absent in 18, deficient in 31, excessive in 12, and normal in 3. He noted that the gastric secretions were diminished or absent in most cases of long standing, while in the few instances where those juices were increased the cases were acute.

In a study of 55 cases of pellagra, Tucker⁸ reported an increase in indican in 3 cases. In the report of the Illinois Pellagra Commission, however, Ormsby and Singer noted a marked reaction for indican in all the cases examined.

The experiments here reported were made upon the patients sent to the Post-Graduate Hospital by the Thompson-McFadden Pellagra Commission. We have endeavored to make a fairly extensive study of the metabolism in pellagra, because a thorough knowledge of the fundamental processes of metabolism appeared particularly desirable in this disease; and, further, because it was believed that points of attack might be disclosed which would offer opportunities for more intensive study.

METHODS EMPLOYED. The general procedures employed in this metabolism study were to secure gastric contents (after the Ewald-Boas meal) as soon as practical after the admission of the patient to the hospital. Subsequently the patient was placed upon a weighed diet, and the urine and feces collected daily for a period varying usually from seven to ten days. Following this period, gastric contents were again secured in certain of the cases, while in two instances a second metabolism experiment was conducted.

The examination of the gastric contents has been directed particularly to determining the acidities and ascertaining the peptic activity. The customary titration methods were employed for the acidities and Rose's method for pepsin, as conducted in this laboratory.⁹

During the period of the metabolism study a lacto-vegetarian and practically purin-free diet was employed for experimental reasons. The general type of the diet may best be illustrated by a sample day (August 8) taken from Case VIII (M. T.).

⁸ Jour. Amer. Med. Assoc., 1911, lvi, 246.

⁹ Post-Graduate, 1912, xxvii, 506.

	Grams or c.c.
Breakfast:	
Corn-flakes	25
Banana	89
Bread	63
Egg	48
10.30 A.M.	
Water	150
Apple	105
Dinner:	
Apples	125
Water	50
Bread	127
Egg	43
Potato	140
3.00 P.M.	
Graham crackers	26
Supper:	
Cream of wheat	25
Water	300
Bread	101
Egg	46
Orange	148
Water	200
10.00 P.M.	
Banana	97
Distributed between the various meals as desired:	
Cane sugar	63
Milk	800
Butter (salt free)	23
Salt (pure NaCl)	6

This would furnish 91 grams protein ($14.6 \text{ N} \times 6.25$), 71 grams fat, 460 grams carbohydrate and would yield approximately 2800 calories, which is not far from the average found for the period in this case.

As insufficient time prevented our making a complete analysis of the food intake, the figures for protein, carbohydrate, and fat were for the most part calculated from the data given by Atwater and Bryant¹⁰ for American food materials, while the figures for the mineral constituents were taken from results compiled by Sherman.¹¹ Many of the figures for nitrogen, however, were from our own analyses, and we believe that the results which we have given for the nitrogen intake are reliable. The protein intake has been calculated from the nitrogen figures by employing the factor 6.25, and the calorific intake obtained by multiplying the grams of protein and carbohydrate by 4 and the grams of fat by 9 and adding these results.

¹⁰ United States Dept. Agri., Office of Exper. Sta., Bulletin 28, Revised, 1906.

¹¹ Chemistry of Food and Nutrition, 1911, p. 332.

Previous to beginning the metabolism study the patients were placed for several days upon the diet they were to receive during the period of actual examination. The end of the twenty-four-hour urine period was taken as 7.30 A.M. After the excretion of the last sample of urine for the day the patients were weighed and then given their breakfast. The urine specimens were collected in three-liter glass-stoppered bottles and preserved with a liberal supply of toluene. The urines were taken to the laboratory at 9 A.M., made up to some definite volume (1000 c.c. where possible), and the nitrogenous constituents, the ammonia in particular, determined in most cases the same day. At this time the qualitative and microscopic examinations were made. The urines were then refrigerated at 0° C. for future use. The feces were collected in weighed tin pails, the weight of the feces ascertained by difference, and then kept in a common receptacle in the refrigerator at -4° C. until the end of the period. In most of the experiments the feces of the experimental period were marked off with charcoal, though in some of the later experiments carmin was employed. When the feces for the whole period had been assembled, they were thoroughly mixed and a weighed portion, generally one-half, dried over the water-bath with the addition of alcohol acidified with dilute sulphuric acid, and subsequently ground to a fine powder. All determinations with the exception of the indol and skatol were made upon the air-dried feces.

The examination of the urine included the usual qualitative tests—namely, tests for albumin, sugar, acetone diacetic acid, and a microscopic examination of the centrifugalized sediment, and, in addition, quantitative estimations of the total nitrogen, urea, ammonia, uric acid, creatinin, creatin, chlorides, phosphates, inorganic and ethereal sulphates, neutral sulphur, total acidity, and indican on the individual specimens, and determinations of sodium, potassium, calcium, and magnesium on composite samples. The methods employed were: For total nitrogen, Kjeldahl; for urea, the Benedict (S. R.) method;¹² for ammonia, uric acid and creatinin, the Folin methods;¹³ for creatin, the Benedict (F. G.)-Myers' modification of the Folin method;¹⁴ for chlorides, the Volhard-Arnold method; for phosphates, uranium nitrate; for inorganic and ethereal sulphates, the Folin methods;¹⁵ for neutral (total) sulphur, Benedict's (S. R.) method;¹⁶ for total acidity, Folin's method; indican as described by Myers and Fine;¹⁷ the sodium and potassium in part as directed by Folin,¹⁸ the potassium

¹² Jour. Biol. Chem., 1910, viii, 405.

¹³ Amer. Jour. Phys., 1905, xiii, 45.

¹⁴ Ibid., 1907, xviii, 397.

¹⁵ Jour. Biol. Chem., 1905-6, i, 131.

¹⁶ Ibid., 1909, vi, 363.

¹⁷ Post-Graduate, 1912, xxvii, 1144.

¹⁸ Handbuch der Biochemischen Arbeitsmethoden, 1911, v, Pt. 1, 292.

being estimated by the Drushel cobaltinitrite¹⁹ method, and calcium and magnesium as described by McCrudden,²⁰ the calcium being estimated volumetrically.

The examination of the feces included certain of the simple routine tests and, in addition, estimation of moisture, nitrogen, fat, carbohydrate, mineral constituents, and the putrefactive products, indol and skatol. The moisture was obtained from the difference in the weight of the moist and air-dried feces. The nitrogen in the air-dried feces was estimated by the Kjeldahl method, the fat on the thoroughly dried feces by the Soxhlet method with anhydrous ether, and the carbohydrate with the Allihn method after hydrolysis of the feces as described by Mendel and Fine.²¹ The mineral constituents were estimated in a similar manner to that described for urine. The indol and skatol were determined upon samples of the moist feces, with the aid of Ehrlich's aldehyde.²² The feces slightly acidified with sulphuric acid were subjected to steam distillation until they failed to give a reaction with this reagent. A portion of the distillate was treated with the reagent to the maximum color, extracted with chloroform, and matched up in a Duboscq colorimeter with a similar extract prepared from mixtures of pure indol and skatol, showing the same color as the specimen under examination. It is believed that in this way an approximation of the amounts of both indol and skatol present was obtained.

CASE HISTORIES. A brief history of the cases upon which this study was made follows. A more detailed consideration of the case histories will be taken up in a subsequent paper of this series.

CASE 1.—J. A. (Pellagra Commission, No. 1, Union County). Fairly well nourished man, aged sixty years; lesions rather slight; some scaling on hands; no evidence of diarrhea.

CASE 2.—M. F. (Pellagra Commission, No. 1, Spartanburg County). Thin, pale, rather poorly nourished girl, aged seventeen years; no marked lesions; had had ovariectomy; no evidence of diarrhea.

CASE 3.—M. McH. (Pellagra Commission, No. 2, Spartanburg County). Fairly well nourished woman, aged thirty-seven years; marked erythema on backs of hands and wrists; some erythema on face and mouth; developed acute mania while in hospital; strychnoides intestinalis observed; moderate diarrhea.

CASE 4.—C. T. (Pellagra Commission, No. 12, Spartanburg County). Well-nourished woman, aged forty years; very slight scaling on hands; not sufficiently definite for diagnosis; showed marked improvement.

¹⁹ Amer. Jour. Sci., 1908, xxvi, 555; also Myers, Jour. Biol. Chem., 1909, vi, 115.

²⁰ Jour. Biol. Chem., 1909-10, vii, 83; 1911-12, x, 187.

²¹ Ibid., 1911, x, 339.

²² Herter and Foster, Jour. Biol. Chem., 1906, ii, 267.

CASE 5.—R. N. (Pellagra Commission, No. 9, Spartanburg County). Moderately well-nourished woman, aged thirty-two years; some scaling on forearms; had had erythema before coming to hospital; recovered while in hospital.

CASE 6.—M. L. (Pellagra Commission, No. 68, Spartanburg County). Tall, thin, poorly nourished woman, aged thirty-six years; said to have had tuberculosis, but no evidence of this could be found while patient was in hospital; some erythema and desquamation on back of hands; condition cleared up quickly.

CASE 7.—E. C. (Pellagra Commission, No. 113, Spartanburg County). Well-nourished girl, aged twenty-years; marked thickening of palms of hands; extensive desquamation on back of hands, forearms, elbows, dorsal surfaces of feet, on and around knees; irregular girdle of desquamation about waist; erythema not evident; case recovered very quickly.

CASE 8.—M. T. (Pellagra Commission, No. 114, Spartanburg County). Fairly well-nourished girl, aged about eighteen years; little erythema and desquamation on backs of hands and forearms; recovered quickly.

CASE 9.—L. G. (Pellagra Commission, No. 115, Spartanburg County). Tall, thin, poorly nourished woman, aged twenty-eight years; scaling on forearms and backs of hands, also slightly in front of neck; dull mentally, although said to have been bright previous to attack.

CASE 10.—M. S. (Pellagra Commission, No. 21, Spartanburg County). Rather tall, thin, poorly nourished woman, aged twenty-eight years; extensive lesions on backs of hands, forearms, arms, shoulders; girdle of erythema around neck; had ovarian cyst.

CASE 11.—B. B. (Pellagra Commission, No. 158, Spartanburg County). Fairly well nourished woman, aged thirty-three years; slight erythema, desquamation and pigmentation on backs of wrists; lesions did not cover great area; had pulmonary tuberculosis as demonstrated by an examination of sputum.

CASE 12.—A. N. (Pellagra Commission, No. 206, Spartanburg County). Fairly well-nourished woman, aged forty-three years; erythema, pigmentation, and desquamation up to middle of back of forearms.

CASE 13.—C. McC. (Pellagra Commission, No. 170, Spartanburg County). Poorly nourished woman, aged thirty-five years; extensive desquamation and discoloration of skin on backs of hands, forearms, arms, shoulders, and around neck; palms of hands much thickened, also deep fissures at points of fingers; marked diarrhea; mentality evidently low; delusions and hallucinations; recovered.

CASE 14.—W. L. (Pellagra Commission, No. 166, Spartanburg County). Fairly well nourished woman, aged thirty-five years;

mild desquamation on forearms. In this case no complete metabolism study was conducted, though an analysis of a twenty-four hour urine, gastric contents, and a qualitative examination of feces were made.

GASTRIC ANALYSIS. The gastric analyses have shown very interesting results, especially when considered in connection with the indican estimations of the urine. In 8 of the 14 cases free hydrochloric acid was absent. The total acidities were low, and pepsin was generally absent, or present only in small quantity. Though considerable amounts of indican were observed in all cases, the quantity was excessive in those with anacidity, reaching in one case nearly a quarter of a gram a day. To emphasize this relationship the data given in Table I have been arranged in order of the amounts of the average daily indican elimination. This association of high indican elimination, with diminished acidity, is indicative of the strong inhibitory influence of the normally acid gastric juice upon putrefaction in the alimentary canal, or at least a certain type of putrefaction. As may be observed, some of the cases with low indicanuria and with free hydrochloric acid present in the gastric juice have a fairly high elimination of ethereal sulphates, but, in general, the total ethereal sulphates as well as the indoxyl-potassium-sulphate are increased in anacidity. Still another factor which may play a part is the activity of the pepsin, especially in the cases where hydrochloric acid is present. Case 12 (A. N.), with only a slightly subnormal acidity, but with a low peptic activity, showed an elimination of indican next in amount to the cases with anachlorhydria. In this series of cases, anacidity was found in about the same percentage of cases as reported by Johnson. Cecconi in the 12 cases which he examined made qualitative tests for indican. Though all of his cases showed an absence of free hydrochloric acid, no uniform relation appeared to exist between the anacidity and the indican, if we are to accept the qualitative tests for indican as representative of the quantitative elimination.

FOOD INTAKES. In general the food intakes may be viewed as indicating the general condition of the patients, since they were allowed considerable liberty in the choice of food, and further provided with all they desired. The food intakes, as shown in Table III, amounted in all cases to from 75 to 110 grams of protein (12 to 18 grams of nitrogen) and 2300 to 3000 calories per day, with the exception of Case 2 (M. F.), during the first period of observation, and Case 3 (M. McH.) during both periods of observation. With the same exceptions all the cases showed a decided plus nitrogen balance during the period of observation, the degree of nitrogen retention being in proportion in general to the gain in weight as shown in the tabulated results. Case 2 (M. F.) during

the first period of nine days, with an intake of 8.9 grams of nitrogen, showed a slight plus daily balance of 0.6 gram, though a decided plus balance was observed with the gain in weight during the second period. Case 3 (M. McH.), with a nitrogen intake of 5.0 grams during the first period, showed a minus daily balance of 1.4 grams, with a decided loss in weight. During the second period, with a nitrogen intake of 7.2 grams, she gained slightly in weight and showed a plus daily balance of 1 gram nitrogen. Corn in the form of corn-flakes was consumed in all the experiments, while case 2 (M. F.) ate considerable quantities of corn-bread during the second period of observation. During this period of seven days she gained four pounds in weight, showed an average daily nitrogen balance of plus 4.1 grams, and otherwise showed general improvement.

TABLE I.—Gastric Analyses in Comparison with Certain Data of Urine and Feces. Tabulated in Order of Indican Elimination.

Patient.	Gastric analyses.					Urine.			Feces.	
	Volume of contents.	Free HCl.	Total acidity.	Lactic acid.	Peptic content ²³ (Rose.)	Indican. Daily average.	Ethereal sulphates as SO ₂ . Daily average.	Ratio ethereal to inorganic SO ₂ .	Indol. Daily average.	Skatol. Daily average.
13—C. McC.	C.c.					Mg.	Mg.		Mg.	Mg.
4—C. T.	270	0	5	+	0.5	240	181	1 to 8	—	—
	90	0	8	++	0	208	194	1 to 7	5	10
	180	0	7	++	0					
1—J. A.	50	0	6	++	0					
	94	0	4	++	0	151	207	1 to 6	0	28
2—M. F.	130	0	4	++						
	135	0	14	++	0	128	126	1 to 8	0	2
9—L. G.	60	0	12	++	0	48	98	1 to 11	3	3
	70	0	12	++	0	95	203	1 to 6	11	34
3—M. McH.	200	0	4		1					
	188	0	7	+	2	69	97	1 to 7	2	9
8—M. T.	3	0	—		—	91	122	1 to 5	7	7
	140	0	20	++	7					
11—B. B.	140	0	8	++	0	88	161	1 to 11	3	12
	300	0	4	+	2	71	126	1 to 11	21	51
12—A. N.	65	18	43	..	0.5	65	124	1 to 17	Tr.	Tr.
	20	36	60	..	0.5					
14—W. L.	90	40	64	..	7	57	—	—
6—M. L.	135	15	32	+	7	45	149	1 to 11	0	1
	35	22	42	..	5	43	59	1 to 20	14	0
5—R. N.	270	14	35	..	10					
	45	26	54	+	7					
10—M. S.	170	8	26	..	16	23	117	1 to 11	2	19
	57	2	20	+	2					
7—E. C.	340	17	34	+	2	21	147	1 to 8	0	16

As the tabulated data show the food intake, with the few exceptions mentioned, was generally up to the standard set by Atwater, and thus far above the minimum figures given by Chittenden. Both the protein and the calorific intake appear to have been

²³ Normally the peptic activity of the gastric juice after the Ewald meal is 8 to 11 by the Rose method.

ample as judged by these standards, though perhaps the proportion of fat to carbohydrate is a little higher than ordinarily found.

These data hardly allow of comparison with the results observed by Wussow and Grindley²⁴ at the Peoria State Hospital, for the reason that, with one exception, they were all women and, further, were below the normal average weight. At Peoria they found the general diet supplied per man per day: Protein, 73.5 grams; carbohydrate, 444 grams; fat, 56 grams; energy, 2568 calories; mineral matter, 23.23 grams, of which 1.07 grams were phosphorus; while the corn diet gave protein, 87.2 grams; carbohydrate, 463 grams; fat, 79 grams; energy, 2898 calories; total mineral matter, 27.91 grams, of which 1.64 grams were phosphorus. In general the diet of our patients appeared to furnish a somewhat larger amount of protein and fat, but a smaller amount of carbohydrate. The diets employed by Camurri are likewise of interest in this connection. His mixed diet contained 131 grams protein, 430 grams carbohydrate, 66 grams fat, 24.85 grams mineral matter, and had an energy equivalent of 2600 calories, while his corn diet contained 96 grams protein, 617 grams carbohydrate, 64 grams fat, 26.45 grams mineral matter, and furnished 3450 calories. Camurri calls attention to the small relative amounts of sodium and calcium furnished by certain dietaries. The figures which we have calculated for the salt intake would appear to indicate that in this particular our diet was adequate and well balanced.

COMPOSITION OF THE URINE. The discussion of the urine can best be prefaced by the general statement that the chemical composition of the urine in pellagra does not markedly differ from what one might observe in other individuals of a similar physical condition, except in one particular, the increase in the quantity of the bodies derived from intestinal putrefaction—namely, the ethereal sulphates, and especially the indican. It is perhaps of some significance that a few hyalin casts were observed in 6 out of the 14 cases, while in 2, traces of albumin were detected.

The volume of urine eliminated and the specific gravity gave figures such as one might have anticipated with the fluid and food intake, the average volumes varying between 300 and 1800 c.c., with specific gravities of 1.029 to 1.013. As shown in Table II, the figures for total acidity, chlorides, phosphates, inorganic sulphates, neutral sulphur, for the mineral elements, calcium magnesium, sodium, and potassium (figures for sodium and potassium not included in table) are such as one might expect under the given dietary conditions, and the same may be said in regard to the various nitrogenous constituents.

²⁴ Report of the Pellagra Commission of the State of Illinois, 1911, p. 197.

TABLE II.—Summary Table. Average Daily Composition of the Urine.²⁵

Patient.	Severity of condition.	Sex.	Age.	Wt. at beginning of experiment.	Weight at end of experiment.	Average weight.	Length of experiment.	Date, 1912.	Volume of urine.	Specific gravity.	Qualitative and Microscopic examination of urine.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Undetermined N.	Creatinin coefficient.
1—J. A.	Moderately severe; chronic	M.	60	143	145	68.3	9	June 14 to 23	Ce. 912	1.019	Occasional granular casts, occasional leucocytes.	Gms. 9.40	Gms. 7.68	Gm. .51	Gm. .08	Gm. .36	Gm. .02	Gms. 0.75	5.5
2—M. F.	Moderately severe; chronic	F.	17	76	75	34.2	9	June 9 to 18	676	1.023	Faint trace of albumin on several occasions, moderate number of pus cells.	Gms. 7.74	Gms. 6.75	Gm. .25	Gm. .06	Gm. .20	Gm. 0	Gms. 0.48	5.8
2—M. F. Period 2	Moderately severe; chronic	F.	17	78	82	36.3	7	June 29 to July 6	877	1.020	Negative.	Gms. 7.25	Gms. 6.07	Gm. .30	Gm. .05	Gm. .22	Gm. 0	Gms. 0.61	6.1
3—M. McH.	Severe; acute	F.	37	88	85	39.0	10	June 9 to 19	304	1.028	Moderate number pus cells.	Gms. 5.89	Gms. 4.73	Gm. .33	Gm. .06	Gm. .21	Gm. .04	Gms. 0.52	5.4
3—M. McH. Period 2	Severe; acute	F.	37	85	86	38.1	7	June 29 to July 6	318	1.029	Moderate number pus cells.	Gms. 4.87	Gms. 3.85	Gm. .21	Gm. .07	Gm. .22	Gm. .01	Gms. 0.51	5.8
4—C. T.	Mild; chronic	F.	40	121	122	54.9	9	July 7 to 16	1439	1.018	Negative.	Gms. 9.47	Gms. 7.75	Gm. .50	Gm. .08	Gm. .35	Gm. .02	Gms. 0.77	6.4
5—R. N.	Moderately severe; chronic	F.	32	87	88	39.7	9	July 7 to 16	1198	1.019	Occasional hyaline casts on one day.	Gms. 8.05	Gms. 6.09	Gm. .41	Gm. .08	Gm. .23	Gm. .09	Gms. 1.15	5.8
6—M. L.	Moderately severe; chronic	F.	36	94	100	43.8	9	July 21 to 30	1256	1.019	Negative.	Gms. 10.71	Gms. 8.94	Gm. .56	Gm. .09	Gm. .30	Gm. 0	Gms. 0.82	6.9
7—E. C.	Moderately severe; acute	F.	20	145	150	66.9	7	August 5 to 12	1496	1.014	Occasional hyaline casts on two days.	Gms. 8.08	Gms. 6.50	Gm. .41	Gm. .13	Gm. .33	Gm. .01	Gms. 0.70	4.9
8—M. T.	Mild; acute	F.	18	116	118	53.1	7	August 5 to 12	1444	1.017	Occasional hyaline casts on one day.	Gms. 10.62	Gms. 9.08	Gm. .49	Gm. .13	Gm. .36	Gm. 0	Gms. 0.56	6.8
9—L. G.	Moderately severe; chronic	F.	28	114	118	52.0	8	August 17 to 25	1393	1.015	Trace of albumin on first three days and occasional hyaline casts on first five days.	Gms. 9.12	Gms. 7.55	Gm. .48	Gm. .11	Gm. .26	Gm. .03	Gms. 0.69	5.0
10—M. S.	Severe; chronic	F.	28	89	91	41.3	10	August 17 to 27	839	1.023	Negative.	Gms. 8.64	Gms. 7.24	Gm. .47	Gm. .11	Gm. .23	Gm. 0	Gms. 0.59	5.6
11—B. B.	Mild; chronic	F.	33	90	94	41.7	7	August 23 to 30	987	1.017	Moderate number pus and red blood cells observed on several days and an occasional hyaline cast on one day.	Gms. 8.80	Gms. 7.59	Gm. .41	Gm. .05	Gm. .21	Gm. .02	Gms. 0.52	5.0
12—A. N.	Mild; acute	F.	43	91	95	42.2	7	September 12 to 19	1833	1.013	Negative.	Gms. 12.88	Gms. 10.92	Gm. .35	Gm. .05	Gm. .25	Gm. 0	Gms. 1.31	5.9
13—C. McC.	Severe; chronic	F.	35	70	72	32.0	2	September 18 to 20	646	1.019	Many pus cells.	Gms. 9.45	Gms. 7.66	Gm. .67	Gm. .14	Gm. .11	Gm. .11	Gms. . .	4.4

²⁵ The tables of the individual metabolism studies from which these average figures have been computed will be included in the preliminary report of the Pellagra Commission and the authors' reprints of this paper. For the sake of brevity they have been omitted here.

TABLE II (CONCLUDED).—Average Daily Composition of the Urine.

Patient.	In percentage of total nitrogen.						Urea.	Ammonia.	Uric acid.	Creatinin.	Creatin.	Total acidity terms n/10 acid.	Calcium as CaO.	Magnesium as MgO.	Chlorides as NaCl.	Phosphates as P ₂ O ₅ .	Inorganic sulphates as SO ₃ .	Ratio ethereal: Inorganic SO ₃ .	Ethereal sulphates as SO ₃ .	Neutral sulphur as SO ₃ .	Indican (Indoxyl- potassium- sulphate).
	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Undeter- mined N.															
1	81.7	5.4	0.9	3.8	0.2	8.0	16.5	Gm.	24	Gm.	0.06	429	Gm.	.13	6.08	2.01	1.352	1 to 6	Gm.	.213	151
2	87.2	3.6	1.2	3.0	...	8.5	14.5	Gm.	18	Gm.	.54	303	Gm.	.08	5.14	1.85	1.067	1 to 8	Gm.	.203	97
3	80.3	5.6	1.0	3.9	.7	8.8	13.0	Gm.	15	Gm.	.59	0	Gm.	.07	4.88	2.04	1.064	1 to 11	Gm.	.283	48
3	79.1	4.3	1.4	4.6	.2	10.5	8.3	Gm.	18	Gm.	.57	12	Gm.	.08	1.73	1.36	.705	1 to 7	Gm.	.122	69
4	81.8	5.3	1.8	3.7	.2	8.2	16.0	Gm.	21	Gm.	.59	03	Gm.	.15	3.21	2.09	.577	1 to 5	Gm.	.154	91
5	75.7	4.3	1.0	2.9	1.1	14.2	13.1	Gm.	61	Gm.	.94	06	Gm.	.18	14.05	1.332	1.332	1 to 7	Gm.	.194	208
6	83.5	5.2	1.8	2.8	...	7.7	13.2	Gm.	50	Gm.	.62	28	Gm.	.17	14.07	2.16	1.150	1 to 20	Gm.	.108	43
7	80.4	5.1	1.6	4.1	1.1	8.7	13.9	Gm.	68	Gm.	.81	0	Gm.	.07	12.90	1.88	1.635	1 to 11	Gm.	.149	45
8	85.5	4.9	1.3	3.4	...	5.3	16.2	Gm.	50	Gm.	.03	353	Gm.	.25	8.98	2.17	1.189	1 to 8	Gm.	.280	21
9	82.8	5.3	1.2	3.6	.3	7.5	16.5	Gm.	60	Gm.	.97	0	Gm.	.13	9.83	1.92	1.727	1 to 11	Gm.	.161	88
10	83.8	5.2	1.3	2.7	...	8.8	15.5	Gm.	58	Gm.	.70	09	Gm.	.18	9.40	1.92	1.275	1 to 6	Gm.	.203	95
11	86.8	4.7	1.6	2.4	.5	6.9	16.3	Gm.	57	Gm.	.62	0	Gm.	.12	9.46	2.12	1.270	1 to 11	Gm.	.279	23
12	84.8	5.4	.4	2.0	1.2	10.1	17.7	Gm.	15	Gm.	.57	43	Gm.	.30	6.94	2.21	1.374	1 to 11	Gm.	.270	71
13	81.0	7.1	...	1.5	16.4	Gm.	43	Gm.	.35	367	Gm.	.09	4.50	3.36	2.156	1 to 17	Gm.	.446	65
		7.1	...	1.5	16.4	Gm.	81	Gm.	Gm.	.25	4.50	2.17	1.462	1 to 8	Gm.	.208	240

TABLE IV.—Average Daily Composition of the Feces.

Patient.	Moist feces.	Air dry feces.	Moisture.	Nitrogen.		Ether extract.	Ether extract.	Fat utilization.	Carbohydrate as glucose.		Carbohydrate utilization.	Ash.	Ash.	Calcium as CaO.	Magnesium as MgO.	Phosphates as P ₂ O ₅ .	Chlorides as Cl.	Indol.	Skatol.
	Gms.	Gms.	Per cent.	Gms.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Gms.	Gms.	Gm.	Gms.	Gms.	Mgms.	Mgms.
1—J. A.	103	21.6	79	1.01	4.67	6.9	31.9	94	.6	2.57	99.8	4.49	3.06	1.40	.25	1.09	.23	0	28
2—M. F.	56	13.7	76	.51	3.71	3.2	23.2	96	.4	2.77	99.8	3.06	3.06	1.26	.18	.71	.06	0	2
2—M. F.	90	23.6	74	1.13	4.81	2.7	11.4	98	.9	3.62	99.7	4.95	4.95	2.00	.31	1.01	.11	3	3
Period 2																			
3—M. McH.	59	9.7	84	.54	5.53	2.1	21.7	94	.2	2.57	99.8	2.16	2.16	.80	.12	.62	.15	2	9
3—M. McH.	182	22.0	88	1.36	6.27	3.2	14.6	95	1.7	7.57	99.0	3.96	3.96	1.08	.26	.76	.42	2	7
Period 2																			
4—C. I.	113	24.4	78	1.49	6.10	4.5	18.3	95	.6	2.53	99.8	5.05	5.05	1.94	.33	1.39	.38	5	10
5—R. N.	233	36.4	84	2.35	6.45	2.9	8.0	98	3.3	9.00	99.0	5.08	5.08	2.17	.35	1.17	.85	14	0
6—M. L.	73	19.0	74	.75	3.97	4.5	23.7	97	.8	4.14	99.7	4.52	4.52	1.75	.34	1.44	.14	0	1
7—E. C.	148	28.6	79	1.84	6.43	6.4	22.2	96	1.1	4.05	99.6	4.49	4.49	1.70	.20	1.16	.43	0	16
8—M. T.	129	23.1	82	1.49	6.46	4.4	19.2	94	.9	4.00	99.8	3.74	3.74	1.49	.25	.97	.33	3	12
9—L. G.	200	31.0	85	1.47	4.75	10.9	35.2	91	1.2	3.90	99.6	5.86	5.86	1.99	.33	1.49	.26	11	34
10—M. S.	195	22.8	88	1.10	5.98	3.3	14.3	92	1.3	5.67	99.5	4.33	4.33	1.44	.30	.88	.40	2	19
11—B. B.	367	41.1	89	2.28	5.55	10.5	25.5	92	1.4	3.36	99.5	7.15	7.15	2.40	.40	1.60	.67	21	51
12—A. N.	147	27.4	81	1.41	5.13	5.3	19.4	96	1.2	4.53	99.6	5.84	5.84	2.65	.43	1.03	.41	Faint	0
13—C. McC.	772	42.0	95	2.70	6.44	11.1	26.3	89	Trace	Trace	100.0	11.47	11.47	2.47	.36	2.44	2.19	0	0

The elimination of total nitrogen, urea, ammonia, uric acid, and creatinin is perhaps slightly below the so-called normal, though the constituents dependent upon exogenous factors, namely, the urea and ammonia, are in accord with the diet, and those of endogenous origin, namely, the uric acid and creatinin, are such as might be observed in other individuals of similar physical condition. Since Folin²⁶ first considered the distribution of the nitrogenous constituents in normal urine a large amount of work has been done on this subject. The large amount of data collected in the publications of the Referee Board²⁷ is unusually good confirmation of the statements of Folin in this particular. Although our data for the percentage of ammonia and undetermined nitrogen are slightly above the so-called normal figures and the other constituents slightly below, these differences are readily interpreted as due to the diet and the physical condition of the patients. As Folin has so well shown, with a reduction of the nitrogen-intake the urinary constituents of exogenous origin necessarily form a smaller percentage of the total nitrogen, and our figures for urea nitrogen, generally 83 per cent., are in accord with the nitrogen of the food. As the endogenous metabolism of the body was at a low state of activity, due to the rather poor physical condition of the individuals, we would hardly expect the uric acid (purin-free diet) and creatinin nitrogen to form an increased percentage of the total nitrogen. On the contrary the percentage of nitrogen in this form is rather below the normal.

An examination of the absolute amounts of the various nitrogenous constituents eliminated by the different individuals shows that in general the urea varied between 10 and 20 grams, the ammonia between 0.3 and 0.8 gram, the uric acid between 0.15 and 0.39 gram, and the creatinin between 0.4 and 1 gram. The absolute amount of the undetermined nitrogen in general falls within normal limits, though, as mentioned above, it forms a rather high percentage of the total nitrogen. In Cases 2 and 12, however, the figures are considerably higher than those found in other cases of the series.

The creatinin elimination is below normal in all cases, this fact being particularly well shown by the creatinin coefficients. Normally, coefficients of 7 to 11 are found, while here the figures vary between 5 and 7. As recently discussed by one of us²⁸ (Myers), the creatinin elimination is lowered in conditions associated with decreased body efficiency. This general inefficiency is further brought out by the fact that 10 out of the 14 cases eliminated creatin, though in only 2 cases was it present in large amount.

The elimination of the mineral constituents hardly requires

²⁶ Amer. Jour. Phys., 1905, xiii, 66.

²⁷ United States Dept. of Agric., Report No. 88, 1909, and No. 94, 1911.

²⁸ AMER. JOUR. MED. SCI., 1910, cxxxix, 256.

further comment, except for that part containing an organic radicle, namely, the ethereal sulphates. Certain of the facts in this connection are best brought out in Table I, in which the data are arranged in order of the amounts of indican eliminated. The absolute amounts of the ethereal sulphates appear to be increased in a few instances, in which case there exists a low ratio to the ethereal sulphates. This is especially pronounced in the cases of anaecidity, in which very large amounts of indican were eliminated. Here the indican appears to parallel the total ethereal sulphates, but apparently for the reason that the indican forms a considerable part of the total ethereal sulphates. The low ratio of inorganic to ethereal sulphates was observed in the cases reported by Camurri.

COMPOSITION OF THE FECES. The examination of the feces as shown in Table IV revealed widely varying conditions as to volume and consistency—watery stools, soft stools, well-formed stools, and hard stools—the average daily elimination amounting to from 60 to 700 grams of moist feces and 20 to 40 grams of air-dried feces, the moisture varying between 75 and 95 per cent. The microscopic examination of the feces has not yielded data of special significance, though in certain cases evidence of digestive inefficiency has been observed, and in some cases considerable mucus, probably in part due to the diarrhea. In several instances strongly positive fermentation tests with Schmidt tubes have been observed, notably in Case 3 (M. McH.), period 2, though the estimation of the carbohydrate content of the feces ought to be a more adequate criterion. The daily fecal nitrogen was found as low as 0.5 gram where the nitrogen intake was low, and as high as 2.7 grams in the reverse condition, accompanied by severe diarrhea. These figures fall within the normal limits, however, and the percentage of nitrogen in the air-dried feces cannot be said to be excessive, though perhaps slightly above the normal average in a few cases. In 3 cases (Case 3, period 2, Case 5, and Case 13) the so-called protein utilization was below the other figures observed, but probably in part due to the diarrhea. The daily fat eliminated varied from 2 to 11 grams, with percentages of the air-dried feces ranging between 8 and 35 per cent. The fat utilization was good in all cases, though the figures for Cases 9, 11, and 13 were slightly below that observed in other cases. The figures for the carbohydrate were from direct estimation, and are therefore much more reliable than the results generally reported as determined by difference. The tabulated data show that the utilization was 99.5 to 99.8 per cent. in all but 2 cases (Case 3, period 2, and Case 5), where the utilization was 99 per cent. and the percentage content in the feces 7.6 and 9 per cent. These results show quite conclusively that the ability of the pellagrins to absorb their food is only slightly if at all impaired and that this is in part due to the diarrhea. The data on the feces

reported by Camurri bring out similar points, though he has only five sets of average figures with which to make comparison.

The examination of the feces has included quantitative determinations of calcium, magnesium, phosphates, chlorides, as shown in Table IV, and also of sodium and potassium. These data have not revealed any apparent derangement of mineral metabolism, though certain interesting relationships have been brought to light, which will be presented in a subsequent paper.

The feces of pellagrous individuals have a most characteristic aromatic odor, and the estimations of the indol and skatol would indicate that this odor was due to the large amounts of these aromatic bodies found to be present. Normally only traces of these bodies are present, and from the investigation of Herter²⁹ and also of one of us³⁰ (Myers), with Fisher and Diefendorf, the amounts detected, especially of skatol, may be regarded as decidedly abnormal and indicative of peculiar bacterial conditions in the intestine. When these results are compared with the acidity determination in the gastric juice, some relation between the amount of skatol formation and anacidity is apparent.

SUMMARY. The ability of individuals suffering from pellagra to utilize the various foodstuffs as indicated by our series of fifteen experiments appears to be only slightly if at all below the normal.

The elimination of mineral and nitrogenous constituents in the urine is such as would be anticipated under the dietary and physical conditions of the individuals. A lowered physiologic efficiency is indicated by the low creatinin coefficients and the elimination of small amounts of creatin in the urine. The presence of a few hyalin casts in about 45 per cent. of the cases points to some possible irritation of the kidney.

Anacidity is a condition common in pellagra, found in eight of our fourteen cases. It is generally associated with an entire absence of pepsin, or with pepsin in only very minute quantities.

Individuals suffering from pellagra show a marked indicanuria, which is excessive in the cases with gastric inefficiency. Though the ethereal sulphate hardly parallels the indoxyl-potassium sulphate, the quantities eliminated are much higher where anacidity exists and they furthermore hold a higher ratio to the inorganic sulphates.

The feces contain decidedly abnormal amounts of indol and skatol, especially the latter.

The presence of excessive amounts of indican in the urine, associated with a high elimination of ethereal sulphates, when considered in connection with the abnormal amounts of indol and skatol in the feces, points to some unusual bacterial conditions in the intestine. From the data at hand this putrefaction would appear to take place rather high up in the intestine.

²⁹ Bacterial Infections of the Digestive Tract, 1907, p. 239.

³⁰ Zentralbl. f. Stoffwechsels, 1908, ix, 849; Amer. Jour. Insanity, 1909, lxx, 607.

ACUTE SUPPURATIVE LYMPHADENITIS, ABDOMINAL, DUE
TO A DIPLOSTREPTOCOCCUS: AUTOPSY.

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WITHIN the last two years the number of infections due to diplococci and diplostreptococci has greatly increased. Many of these infections are quite serious and not a few are fatal. The organisms described in various parts of the country are similar and likewise are the diseased conditions produced. That these infections are on the increase cannot be explained on the basis that they were not recognized heretofore because of the unusual sites of the lesions.

In this city and surrounding country, during the spring of 1912, there occurred many infections of this nature. The majority of the lesions were located in the cervical lymph nodes and the periglandular tissue. Practically all of them followed throat infections. Many cases subsided without suppuration, but in a number drainage was necessary. The pus from all of these cases showed enormous numbers of short chain diplostreptococci which were Gram positive. They grew on blood serum as small isolated white colonies. On blood agar quite a large hemolytic ring was produced around each colony. The organisms lived only a few days on artificial media, and the colonies rarely developed larger than the head of a pin.

On May 12, 1912, I was called to see the patient, Mr. R. S. The history as taken by Dr. F. G. Nifong, in whose surgical service the case occurred, is as follows:

The patient was aged forty-one years; American; farmer; male; white; widower.

Family History. Father living and in good health, eight-one years old. Had seven brothers and two sisters. One sister and two brothers are dead. One uncle died from cancer.

Previous History. Never had any serious sickness in his life. Three years ago he fell from a tree and sustained some internal injury.

Present Trouble. On May 1 he suffered epigastric pain and a little nausea after breakfast. He ate his dinner and suffered severely after it. The next day he called Dr. R. W. Berry, of Mexico, Missouri. Castor oil was administered and the bowels moved freely. Pain continued, and on May 12 the patient visited Dr. Berry in Mexico, which is fifteen miles from his home. At this time the patient was suffering from severe pain in the region of the gall-bladder, and there was some jaundice. After staying one night in Mexico he returned to his farm. He suffered greatly

in returning, and from this time on he had increasing pain. Since that time he has suffered a great deal, especially after eating, and has been rapidly declining.

Physical Examination. The chest is negative. There is marked muscle resistance all over the abdomen, and especially over the epigastric region. A small area just below the umbilicus was more tender than other parts of the abdomen.

The temperature upon admission to the hospital was 101°, but dropped to normal a few hours after being put to bed. From that time until death his temperature never registered over 100. The white blood count was 14,000. The pulse ranged from 68 to 78. Throughout the illness the patient perspired very freely.

On May 27 the patient was operated and the following notes were given by Dr. Nifong: Median incision. Could find nothing in the colon or stomach. The appendix was removed and showed some evidence of inflammation. After raising the stomach and colon much induration of the mesentery and great enlargement of retroperitoneal and mesenteric lymph nodes were noted. This condition was especially noticeable in the mesojejunum. The abdomen was then closed.

The patient gradually grew weaker, and died June 6. An autopsy was immediately performed and the following is a summary of the findings: The body of a greatly emaciated white man. The skeletal system is moderately heavy and the musculature very light. The subcutaneous fat is practically absent. The lungs are free from adhesions, containing air throughout. They are normal except for a little scarring at the right apex. The heart is normal, all of the valves are delicate. The spleen is normal. All of the mesenteric and retroperitoneal lymph nodes are greatly enlarged and are quite soft. Upon section a greenish-yellow pus escapes. The largest of these lymph nodes are in the duodenal and ileocecal regions. The mesentery is indurated. The liver is somewhat enlarged, and upon section shows numerous abscesses varying in size from a pinpoint to 1.5 cm. in diameter. The abscesses are filled with a greenish-yellow pus and are located in connection or in apposition to the bile ducts. The gall-bladder is normal. The kidneys are slightly enlarged, and on section are found to contain a great deal of blood.

Anatomic Diagnosis. Acute suppurative lymphadenitis affecting practically all of the abdominal and pelvic lymph nodes. Acute suppurative hepatitis, with abscess formation.

A histologic study of the tissues showed the condition to be of an acute suppurative type. Examination of the smallest hepatic abscesses showed that they were not in connection with the bile ducts but in the tissue immediately surrounding the ducts. The infection had apparently been conveyed by the lymphatics. Smears from the pus showed enormous numbers of organisms belonging to

the diplococcus or diplostreptococcus type. These organisms occurred in pairs and in chains of four or six. They were Gram positive.

After the autopsy an attempt was made to find if the individual had suffered from a throat infection previous to this illness. He mentioned no such trouble in the histories given to Dr. Berry or Dr. Nifong. Whether or not the condition was secondary to a throat infection I am unable to say. The organism causing it was the same as occurred in the cervical lymphadenitis cases and the lesions were of the same kind. Surely a primary lesion had occurred somewhere in the respiratory or alimentary tracts, but it could easily have disappeared before the examinations were begun, or was so slight as to escape the notice of the patient.

OCCUPATIONAL BRASS POISONING: BRASS-FOUNDER'S AGUE.

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INTRODUCTION AND DEFINITIONS. 1. *The Alloys.* Brass is an alloy composed of copper and zinc. Fine brass or red brass contains two parts of copper and one part of zinc. However, as these two metals combine in practically all proportions many alloys are possible. As zinc is by far the cheaper of the two component metals its percentage in the alloy is likely to be much increased until a so-called yellow brass is produced in which the zinc component may be from 40 to 50 per cent. This the workmen style "cheap yellow brass."

Bronze is an alloy consisting of copper and tin. Usually the copper component is about nine parts to one part tin. In the industry, however, red brass is very often styled bronze, although zinc is the other component instead of tin. It is only rarely that these two or three metals are used exclusively in the particular alloy to be made, but for the purpose of conveying certain physical properties to the casting, certain other metals are added, such as lead, aluminum, phosphorus, nickel, and antimony. There are some threescore of these various compositions which are well known and are made up for certain purposes, brass, bronze, German silver, aluminum alloys, type-metal, etc.

In the usual foundry practice these various alloys are not made by putting in certain proportions of the various metals, but, as a rule, a large percentage, from one-third to one-half on the average, of scrap brass, copper, and bronze, consisting of all sorts and com-

positions of metal, gathered up usually by junk dealers, is melted down, and then a small portion of the proper copper, zinc, or nickel ingot added to arrive at an approximate composition. In fact, a large amount of the so-called virgin copper, zinc, etc., used is bought from refiners of scrap metal, and the composition is very uncertain. Certain foundries make a specialty of yellow brass castings, others of red brass or bronze castings, others of German silver, etc., while the refiners are concerned with the handling of all of these metals, and usually with a large amount of lead.

Consequently, the brass-manufacturing industry, or more properly the non-ferruginous metal-working trade, is engaged in the handling of large amounts of copper, zinc, and tin, while it must not be overlooked that lead, antimony, nickel, phosphorus, arsenic, and cyanide compounds sometimes enter into these industries, as well as the handling of concentrated and fuming acids, muriatic, sulphuric, nitric, and hydrofluoric.

Finally, scrap metal, old boiler tubes, etc., by the action of air and moisture, may be covered with more or less poisonous oxides and carbonates by which ignorant workmen may be poisoned, both by handling and breathing the metallic dusts. In addition to the metals above named as entering into the composition of various brass alloys, the salts with which they are combined to a limited extent require some notice, such as the oxides, the sulphides, the sulphates, silicates, and nitrates.

2. *Pseudo-brass Poisoning.* Direct toxic effects due to any of these alloys of zinc, copper, etc., in the cold metallic state, when these come in contact with the tissues of the body, are of mechanical traumatic significance only, with whatever possibilities subsequent infection may add. As is well known, also, the salts of some of these metals have a local effect, which is astringent to caustic. The inhalation of dust of any of these alloys, as, for instance, among polishers, buffers, and grinders, in the industry does not produce the symptom-complex known as "brass-founder's ague," which will be described shortly. An investigation made by the Illinois Commission on Occupational Diseases,¹ 1910, among some 2000 brass-polishers and buffers, failed to discover any affections peculiar to brass dust itself, nor did it appear to be any more harmful than iron dust to iron workers, or stone dust to masons and stone-cutters. It is true that these workers suffer from chronic bronchitis in proportion to their exposure, and rapidly develop respiratory affections. According to Lehmann and Saito² the

¹ Report of Commission on Occupational Diseases to His Excellency Governor Charles S. Deneen, Illinois, January 1, 1911. Copies obtainable from State Factory Inspector, Chicago.

² Experimental Untersuchungen über die quantitative Absorption von Staub durch Tiere bei genau bekannten Staubgehalt der Luft, Arch. f. Hyg., 1912, lxxv, S. 134; Lehmann, Saito and Gfroerer. Ueber die quantitative Absorption von Staub aus der Luft durch den Menschen, ibid., S. 152; Murgia, E., Ricerca sull'assorbimento e sulla tossicità di alcuni minerali di zinco, La Clinica Moderna, 1906, xii, 316-19.

great bulk of inspired dust finds its way into the stomach, not into the lungs as has been confidently assumed. Obviously, inhaled dusts are collected in the upper respiratory passages, and either discharged directly therefrom or swallowed, while less than a quarter reaches the lungs. This would be particularly true of these heavier metallic dusts.

The dusts from alloys rich in copper generally produce in workers green-stained hair, a greenish deposit on the teeth and gums, and a green tint to the perspiration, which may persist briefly even after a thorough bath, but all of these are without direct effects upon the health. Such findings are much more pronounced among copper workers than brass-workers. Literature teems with references to the relative harmlessness of copper upon the human organism. It has been found accumulated in all the organs of the body, and even in the bones of former copper-workers, which have shown a green discoloration when later removed from graves. About seventy-five coppersmiths interviewed in Chicago were found to be uniformly healthy. Many of these were old men who had been at the trade from thirty to fifty years. This agrees with the observations of others.

"Brass itch" is a rather common condition among brass-polishers which is due to the slight irritation of brass dust, combined with habits of uncleanness, and is more prevalent in hot weather. Brass-foundrymen, however, are singularly free from these green discolorations of hair, teeth, perspiration, etc., for the obvious reason that they are very little exposed to brass dusts.

3. *Limitation of Brass Poisoning.* Brass poisoning may then be narrowed down, even in the industries, to those exposed to the inhalation of fumes arising from molten brass within the brass foundry. Hence, the affliction "brass poisoning" is unknown outside of the industry. Brass in any condition of temperature short of that of the recent vaporous state of its components, produces no intoxication peculiar to itself.

4. *Brass-founder's Ague* (brass chills; Giessfieber; Staubfieber; fièvre des fondeurs; Gelbgiesser. The workmen use cruder terms, such as "the shakes," "smelters' shakes," and "zinc chills"). This is the theme of interest in occupational brass poisoning. Without question it is a symptom-complex peculiar to the human being. Investigators to date have failed to produce the ague features in lower animals either by inhalation of brass fumes, intratracheal insufflations, ingestion or instillations or injections.

"Brass-founder's ague" may be defined as an acute malaria-like syndrome of chill, fever (sometimes), and sweat, appearing a few hours after the inhalation, for a few minutes or longer, of the vapors or fumes arising from molten brass, or from the fumes of pure zinc alone,³ affecting only or mostly those unaccustomed

³ K. B. Lehmann, Giess-oder Zinkfieber, Arch. f. Hyg., 1910, ed. lxxii, S. 358-381.

to such exposure; further characterized by the development of a form of temporary immunity, and absence of immediate serious or fatal consequences, a lack of definite pathology, and the probability of the development of non-resistance to secondary affections, which account for the increase in the morbidity and mortality of persons so exposed.

The symptoms, which appear usually several hours after the pouring of brass or after an exposure to the metallic smoke arising from the metal, set in with a dry, parched throat, an irritating and unproductive cough, a metallic taste, a feeling of constriction in the chest, lassitude, more or less anorexia, followed occasionally by nausea and sometimes emesis. Within one to four hours chilly sensations begin to be noticeable while a slight dull headache develops. The workman usually lies down or takes to his bed. The chills rapidly increase into a distinct rigor, which may last from a half to two or three hours. No amount of external heat or blankets appears to lessen the rigor. Also, there is a great desire to imbibe hot drinks and stimulants. Accompanying the chills and rigor there are usually muscular cramps and sharp joint pains. The victim feels that he is deathly sick. These symptoms end almost by crisis, and are followed at once by a most profuse perspiration, while the prostration lasts for several hours longer. In many cases there is a distinct rise in temperature during and following the chills, but it is not constant and may be subnormal. It does not usually mount high. Following the stage of perspiration, the victim, quite prostrated, falls into a deep and restful sleep, from which he awakens with no remaining symptoms of his recent experience other than a little exhaustion, perhaps a metallic taste in his mouth, and a temporary loathing of food. The entire attack usually lasts from five to twenty hours; seldom longer.

The pulse during the chill is small and rapid (120 to 130 per minute). The respiratory rate is not much affected. The blood findings during and after a chill have been reported by most investigators as entirely normal, although some have found a slight leukocytosis. The urine after a severe chill invariably shows albumin and casts, which clear up within a day or so. In 1906, J. Sigel⁴ proved the presence of zinc in the urine. This has since been verified by Lehmann, Arnstein, and others. Sigel also proved the absence of carbon monoxid hemoglobin as an etiological factor by spectroscopic examination of the blood. Weyl⁵ comments on associated splenic enlargement. Arnstein⁶ emphasizes the large amount of zinc found in the feces.

⁴ Das Giessfieber und seine Bekämpfung mit besonderer Berücksichtigung der Verhältnisse in Württemberg, *Vrtjschr. f. gerichtl. Med.*, 1906, **xxxii**, S. 174.

⁵ *Handbuch der Arbeiterkrankheiten*, 1908, note, S. 114.

⁶ Arnstein, A., *Beitrag zur Kenntnis des Giessfieber*, *Wiener Arbeiten aus dem Gebiete des sozialen Med.*, 1910, 1. Folge, S. 49-59.

There are many conditions which seem to influence the onset and severity of brass chills. The newer workmen, or those who have returned to work after a week's vacation, perhaps only after a day or so off, as over Sunday, are the most liable. Unless the exposure to the metallic smoke and vapors has been unduly severe, the workman continues at his vocation all day without noticing untoward health effects. It is usually after leaving the workshop at night that the sickness comes on. Many state that as soon as the cold outside air strikes them the chill is inaugurated. Hence the chills are far more common in the winter than in the summer. Many state that while riding in the street cars after the day's labor, or perhaps on removing the clothes to go to bed in the evening after a previous period of indisposition, the chill begins. The men claim that it is because they breathe more vapors in the winter than in the summer that chills are much more frequent in this season. This is because, in an endeavor to keep warm while at work and to keep the furnaces and moulds from "chilling," the windows, doors, and skylights are kept practically closed; hence the fumes fail to escape through their usual routes of ventilation as they do in the summer season.

Brassman's ague occurs almost exclusively among workers in brass foundries, but also in foundries in which zinc, alone or alloyed, is heated to boiling. In Illinois the only process in vogue of reducing crude ores to recover the zinc is one of volatilizing the zinc in huge smelters—the Belgian process. Here an investigation showed that the men working around the smelters occasionally suffered from zinc chills, or "the shakes," as they were wont to call them. They are not as much exposed to the metallic fumes, however, as men who work in brass foundries. Brass chills do not occur in iron foundries nor in bronze foundries. Neither do they occur among galvanizers, the reason being obvious that in this latter process the zinc is only melted and is not ordinarily heated above its point of volatilization. The method of alloying is of great influence, as the frequency of the chill, other conditions remaining the same, is almost in direct ratio to the percentage of zinc contained in the alloy.

About 70 to 80 per cent. only of workmen seem susceptible to the vapors from brass or zinc and experience the chills. Hence some natural immunity seems to exist. Also a tolerance occurs in about 70 to 75 per cent. of workmen who work steadily at the trade. A further 20 to 25 per cent. sicken more or less regularly, but usually not severely. Only in very rare cases do these attacks occur so continually that a change of occupation is necessary. All factors which tend to lower natural vitality are predisposing to brass chills, especially alcoholism, poor quality of food, as is consumed by a large proportion of the foreign workmen, irregular hours, and excesses of all kinds. In addition, weak, anemic individ-

uals, young persons, and women are more subject to brass chills than are robust individuals.

According to Simon⁷ brass-founder's ague is only an acute expression of a chronic malady, and one which rarely or never comes within the range or experience of practising physicians. This question of chronicity is still a disputed point.

5. *Health of Brass-founders.* "The moulders consider the fever so commonplace and matter-of-course—only a few having been exempt and many having had it as much as one hundred times and more—that they do not go or send to the physician on account of same. At all events, physicians, on this account, have rarely had the opportunity of observing brass-founder's ague," Weyl.⁸

According to Simon⁹ the situation is the same in England, and we have found it to be similar in Chicago.¹⁰

In addition to brass-founder's ague, respiratory diseases are very common (chronic bronchitis and pulmonary tuberculosis), while older workmen invariably complain of gastro-intestinal symptoms, such as chronic dyspepsia, biliary trouble, occasionally gallstones; often they are slightly icteroid. Constipation is the rule among them and hemorrhoids are a common complaint. Pyorrhea alveolaris and carious teeth are common. The frequency of anemia, ill-nourishment, and emaciation has long been cited as characteristic of older brass-moulders.

The inducement to alcoholism among the workmen is great because of the chronic pharyngeal and laryngeal irritation from which they suffer. Most of the workmen resort to whisky, although only a few declare that it is antidotal. It is, unfortunately, a traditional remedy. There is no proof of its beneficial effects.

According to Tatham:¹¹ "They sustain a mortality from 'phthisis' which is in excess of that of 'occupied males' by 50 per cent., while they die more rapidly than the average from diseases of the nervous, urinary, and respiratory systems." Our investigations in Chicago in 1910, although not statistical upon this point, discovered a goodly number of young and middle-aged men invalidated by the ravages of consumption.

"If more proof were wanting of the unhealthiness of brass-casters, it would be afforded by the fact that a few years ago, though there were 1200 casters in Birmingham, there were not more than ten over sixty years of age, and in connection with the superannuation fund of the Amalgamated Brass Worker's Association, from which casters could at the age of fifty-five derive

⁷ Oliver's *Dangerous Trades*, 1902, p. 460.

⁸ *Handbuch der Arbeiterkrankheiten*, 1908.

⁹ Loc. cit.

¹⁰ Hayhurst, E. R., *The Brass-moulder's Secret*, The Survey, New York, 1911, No. 26, xxvi, 879-882.

¹¹ Oliver's *Dangerous Trades*, 1902, p. 135.

benefit, it is an appalling fact that there were only three men . . . enjoying this benefit" (Simon).

Practically only young men are found to be employed in the industry in Chicago. Employers gave as a reason for this that the older men (those over forty) became too slow or undependable for the work. The workmen themselves claimed that they were gradually incapacitated from the inhalation of brass fumes combined with the strain of piece-work. By no means the same condition was found to exist among iron-founders, who were engaged in the same identical processes. As is well known the latter continue at their trade until they reach a fair old age.

BIBLIOGRAPHY. Although the literature on the entire subject of brass-founder's ague is very scarce it is not my intention to enter upon more than a brief summary of it here. The affection was confused with malaria until the year 1830, when Thackrah,¹² in England, first described it as a separate affection peculiar to brass-workers. In 1845 it was recognized and described by Blaudet¹³ in France. In 1858 Greenhow,¹⁴ in England, on the basis of his researches, came to the conclusion that "Brass-pourers and doubtless all workmen who deal with zinc vapors are easily attacked with a disease similar to an intermittent fever of irregular type." In Germany, Schnitzer¹⁵ was the first to call special attention to brass ehills in 1862. In 1906 J. Sigel,¹⁶ in Wurtemberg, Germany, sums up the entire literature concerning this peculiar malady and adds the results of his own investigation. In America a few articles have appeared in recent years, usually reports of individual cases, among them being one by Moyer and Lavin,¹⁷ of Chicago, in 1904; also one by Pietrowicz,¹⁸ in 1904. The disease, as well as chronic symptoms of brass-workers, is also commented upon by George M. Kober,¹⁹ of the President's Home Commission, 1908.

Recent literature deals particularly with the experimental side of this peculiar malady, and the investigations of Lehmann,²⁰ Arnstein,²¹ and Kisskalt²² have thrown considerable light upon its nature.

ETIOLOGY. The question of the exact cause of the ague-like symptoms seen among those exposed to brass fumes has been a matter of dispute since the time of Thackrah, some authors claiming it to be an expression of acute copper poisoning, others a zinc

¹² Essay on the Effects of Arts, Trades, and Professions on Health and Longevity, 1830.

¹³ Annales d'hygiène et de méd. lég., 1845, xxxiii, 462.

¹⁴ Med. Chir. Trans., 1862, p. 180.

¹⁵ Preussische Mediz. Zeitung, 1862, S. 198.

¹⁶ Loc. cit.

¹⁷ Chronic Brass Poisoning, Brass-worker's Ague, Medicine, Detroit, 1904, p. 335.

¹⁸ A Case of Brass-moulder's Ague, Jour. Amer. Med. Assoc., 1904, xliii, 465.

¹⁹ Industrial and Personal Hygiene, 1908, p. 49.

²⁰ Loc. cit.

²¹ Loc. cit.

²² Ueber das Giessfieber und verwandte gewerbliche Metaldampfinhalationskrankheiten, Zeitschr. f. Hyg. u. Infektionskrankh., 1912, lxxi, S. 472.

intoxication, others arsenical poisoning,²³ and still others have commented on the presence of lead, cadmium, etc., in the fumes. The question is a difficult one because of the number of contaminating metals and impurities encountered in the process of manufacturing brass.

The volatilization of the metals in making brass is accompanied by a display of blue-green flames, scintillating sparks, and marked deflagration, especially of the zinc component. A white smoke arises above the metals, out of which small snow-like flakes sublime. It is this whitish smoke and its sublimation products that are the cause of brass chills. Many analyses of this smoke and its products have been made, but no two authorities agree on the same findings, as might be expected from the inconstant composition of the alloys producing it. A typical analysis taken from *Dangerous Trades*, by Oliver, 1902, page 456, is as follows:

	Per cent.
Organic matter	39.42
Oxide of zinc	28.82
Oxide of iron	2.78
Copper	1.71
Silicates	9.14
Moisture	9.64
Other matter	8.49
	<hr/> 100.00

Analysis of a similar specimen made for the Illinois Commission on Occupational Diseases²⁴ gave:

	Per cent.
Zinc	44.9
Lead	0.8

Others have reported the presence of cadmium, nickel, sulphur, traces of arsenic, phosphorus, and other metals and acids.

Although zinc has always been held the metal chiefly to blame for brass chills, its necessary combination with copper has been stoutly maintained up to 1905, when Sigel²⁵ first showed brass chills occurring in foundries where no copper or iron could be demonstrated in the sublimation product. Sigel came to the conclusion that the chills were due to the entrance into the system of metallic zinc in the form of zinc dust and *in statu nascendi*.

In the fall of 1910 I found that so-called "zinc chills" existed among the zinc smelters of La Salle County,²⁶ Illinois. The raw ore used consists of zinc blende (sulphide of zinc). These ores contain no copper or arsenic, and only traces of iron, lead, manganese, and magnesium; 31 per cent. of sulphur is present, as well as oxides and silicates, leaving less than 1 per cent. of undetermined

²³ Von Jaksch, *Vergiftungen*, 1897, S. 184.

²⁴ Loc. cit.

²⁵ Loc. cit.

²⁶ Loc. cit.

matter. However, neither sulphur, silicates, nor any of the other metals present are known to produce a chill, fever, and sweat syndrome.

Lehmann²⁷ was the first to succeed in proving that the syndrome could be produced in man by burning chemically pure zinc. He further concludes that the affection is a direct or indirect zinc poisoning. "According to the very small traces of zinc which appear in the urine, to the symptom complex, and to the sudden cessation of the phenomena, the idea seems acceptable that a resorption of the cell contents (bacterial or epithelial), destroyed or changed by zinc, in the respiratory tract, may be the cause of the peculiar sickness. A complication of intoxication with an infection through the entrance of living bacteria is imaginable in the more severe cases, but certainly only as an exception. Zinc is inhaled only as zinc oxide not as zinc vapor."

Recently about the same symptom-complex has been observed in the case of the inhalation of the fumes of other metals, Armit²⁸ finding a similar syndrome in the case of the inhalation of nickel-carbonyl and cobalt fumes. Very little is known as to the actual inhalation of copper fumes, since, like nickel, its boiling point is very high. There is great likelihood, however, that the severe brass chills which workmen suffer in making German silver where it is necessary to fuse nickel (about 1500° C., which is above the boiling point of copper by 200° or 300°), are due as much to inhalation of copper fumes as to those of the associated zinc. Hansen,²⁹ a metallurgical engineer, cites some peculiar effects not unlike those due to zinc, which he attributes to copper fumes produced in an electrolytic process. When we consider the relatively low boiling point of zinc compared to that of all the other metals with which it is alloyed it is easy to see why these symptoms have been so closely associated with zinc, and not, at least in the industries observed in connection with other metals. Boiling points: Zinc 830° C.; copper, 1300° C.; lead, 1450° to 1600° C.; tin, 1600° C.; nickel, iron, and steel all over 1600° C. Melting points: Tin, 232° C.; lead, 327° C.; zinc, 419° C.; copper, 1080° C.; nickel and iron, about 1500° C. Brass itself melts at about 1000° C. Hence it is seen that, with the exception of mercury, whose boiling point is 357° C., but the dangers from the vapors of which are well known, zinc is the only supposedly innocent metal whose boiling point is commonly reached in the industries.

Kisskalt,³⁰ who has been impressed by the *rise in temperature*, occasionally observed in the brass-ague syndrome, has looked up the literature carefully in regard to other metals which have

²⁷ Loc. cit.

²⁸ Toxicology of Nickel Carbonyl, Jour. Hygiene, 1911, vii, 525-551, and viii, 565-600.

²⁹ Copper Poisoning, Metallurgical and Chemical Engineering, No. 2, ix, 67.

³⁰ Loc. cit.

been inhaled, ingested, and injected, and notes significant analogies. After a series of experiments upon rabbits he concludes as follows: "(1) Subcutaneous injections of zinc salts will produce fever; this may account for the same in brass-founder's ague. (2) Inhalation of mercury often causes fever in man and animals, as well as pronounced respiratory symptoms. (3) Also other heavy metals produce the phenomena of brass-founder's ague by inhalation. Vapors of heavy metals inhaled produce more similar symptoms than when taken up by other routes." At another point in his article he makes the following interesting observation: "For a long time it was considered that fever was produced by bacteria only; then it was found foreign proteins had the same effect; now heavy metals come to be added thereto. The effects of all seem to be the same. Heavy metals produce proteid precipitation and so 'denatured' protein occurs in the organism and this produces the fever. Zinc especially causes precipitation in unusual dilution."

In some recent experiments (not yet published) carried on under the Sprague Memorial Institute, Chicago, we have been able, by using Bertrand and Javillier's³¹ calcium zincate method of isolating zinc, and Ganazzini's³² basic urate of zinc test to verify its presence, to trace zinc, in the case of rabbits, which were exposed for as short a time as forty minutes to the inhalation of brass fumes, through the lungs (six hours afterward), and liver and kidneys (twenty-four hours afterward).

It is very probable that the peculiar toxicity of zinc is due, as Armit has found in the case of nickel carbonyl, to its being introduced in a gaseous form, perhaps zinc carbonyl, and that the zinc is deposited as a slightly soluble compound in a very fine state of subdivision over the immense area of the respiratory surface.

SCOPE OF THE BRASS INDUSTRY. In brief this may be said to include all the non-ferruginous metal trades, since the brass furnace is used for melting and alloying practically all metals except iron and steel. Zinc is an almost universal constituent, both because it is cheap and because of the physical properties it bestows upon the alloy.

England, Germany, and France are all great centres of brass manufacture. In America, according to the Bureau of Census³³ the products of the industry exceed \$100,000,000 in annual valuation, of which over 50 per cent. is controlled by Connecticut

³¹ Sur une methode extremement sensible de precipitation du zinc, Bull. de la Soc. Chim. de Paris, 1907, 4a S. T. I., p. 63; Annales de Chimie An. Appl., 1907, T. II, p. 179, and Sur u methode pertant de doser de tres petites quantites du zinc, Compt. Rendu de l'Aead. des Seien., Paris, 1907, T. 145, 2 sem., p. 924.

³² Ricerca qualitativa dello zinco e sua identificazione con una nuova reazione, 1909, Bollettino della Societa Medico-Chirurgia di Pavia, xxiii, 72-90.

³³ Bureau of Census, United States, Department of Commerce and Labor, Special Reports, Manufactures, 1904, Part I, pp. cciv.

manufacturers, with a large part of the remainder in the States of New York, Pennsylvania, Illinois, and New Jersey.

The products of manufacture in this non-ferruginous industry are exceedingly varied and important, such as trinkets, fixtures, and ornaments of all kinds, plumbing, chandelier, bed, automobile, and soda-fountain parts, valves, couplings, nipples; white metal, German silver, gun-metal, bell-metal, type-metal, aluminum and all its alloys, solders, babbitt, pewter, railway car journals, etc.

CHICAGO BRASS MANUFACTURING. In the summer of 1910 there were 182 brass manufacturing concerns inspected in Chicago.³⁴ Of these 89 were found to be engaged in the brass foundry or refining business, representing in all 2212 employees within the foundries. These foundries were found to be located in all manner of places, from basements, midfloors, and top floors in great buildings to specially built foundry buildings.

It was found that skilled labor was employed in the small jobbing and specialty shops almost altogether, whereas the large concerns which were usually making standard type products, had machine moulds and employed large numbers of unskilled foreigners. Women were found to be employed only in core work, usually in small rooms more or less ineffectively partitioned off in one corner of the foundry room. Skilled laborers were found to be mostly Americans, Englishmen, Scandinavians, and Germans. The unskilled, who outnumbered the former by ten to one, were nearly all Polish or Bohemians; 12 of the 89 firms employed union labor only, most of the large concerns were strictly non-union, whereas the balance were said to be "open shop." It was found that the non-union concerns and many of the others were united together in an organization known as the Chicago Brass Manufacturers' Association, which maintained a central office, and had as a not unimportant duty the employing and approving of workmen.

The question of ventilation in these 89 foundries was carefully investigated. It was found that 45 were so situated that surrounding buildings interfered with whatever natural ventilation they had. That in only 6 were the furnaces located in a separate room from the moulding and casting quarters. Only 12 had a separate core room, whereas over one-fourth of the total firms had not provided separate quarters for processes strictly ulterior to foundry work. Practically everywhere only natural ventilation by means of roof apertures, windows, and doors was depended upon to free the foundry quarters from the noxious vapors of molten brass. Only 9 had made any attempt at artificial ventilation, such as suction fans, blow fans, etc. Adequate ventilation, especially as regards any sort of inclement weather, was found to exist in only 22 places, and in none of these could it be considered better than fair.

³⁴ Loc. cit.

Light was found to be good in 50, fair in 21, poor in 17, and artificial only in 1 foundry. Temperature was unduly hot in 25 foundries, whereas it was found that nearly one-half depended upon soft-coal stoves for general room temperature in the winter-time, and not a few upon open salamanders. In many places the general sanitary arrangements, such as facilities for washing, places for changing clothes, toilet rooms, etc., were either lacking or very inadequate, and usually fully exposed to the foundry vapors and fumes.

In no foundry was room space found to be less than 500 cubic feet per person. It is quite evident, however, that foundries should not have their cubic air space measured on the same basis as that of a living room or even a workshop room. The height of roof or ceiling was noted in each foundry, and showed that in 26 it was 12 feet or less. When such was the case with the absence of overhead ventilators the escape of brass fumes from furnaces and during pouring was greatly hampered. In only 2 places were special rooms provided as eating quarters, and it was found that the workmen almost invariably ate their lunches in the foundry room. In most places the first pouring had been completed just before the noon hour, hence the fumes and sublimation products were still in the atmosphere to a greater or less extent at that hour.

There was considerable complaint among many brass moulders of the constant physical and mental strain required at the present day. It was claimed that a foreman or other expert would set a pace on a certain class of work for a few hours or a day's time, after which the men were compelled to keep up to this record, or be docked on the day's pay. The hours of work in practically all places was found to be from 7 A.M. to 5.30 P.M., with a half-hour lunch period.

The amount of exposure to brass fumes varied considerably in different foundries and to some extent with different classes of workmen. In places where pouring was done but twice daily the exposure was minimal, but where it occurred from four to six times daily, each time requiring from ten to thirty minutes to clear the atmosphere, and in several large establishments where pouring was practically continuous all day, there was almost a constant exposure. In the latter places the workmen often sickened before the day was over and had to quit for the day. The winter season was bitterly complained of by many workmen, because of the necessity of closing the means of natural ventilation to prevent chilling of the moulds. As a rule, the furnacemen were the most exposed, and the greatest sufferers.

In places where refining of old scrap metal was done cases of chronic plumbism were occasionally encountered. Also it was found that in nearly all foundries from 0.5 to 7 per cent. of lead was contained in the alloy. Phosphorus was found to be in almost

universal use, but in limited quantities, and no diseases directly traceable thereto were found. In type foundries and refineries there seemed a liability to antimony poisoning, but no cases were discovered.

Other deleterious influences to which brass-founders were exposed were found to be carbon-monoxide gas from improperly ventilated furnaces, and the nauseating odors of burnt oil from oil-blast furnaces. Occasionally, where supplementary processes were carried on in the foundry quarters, the atmosphere was found contaminated with metallic dusts from polishing and buffing, with mineral acid and alkali vapors from cleansing processes and cyanide vapors from plating tanks.

Evidence of occupational disease was closely inquired into at all foundries, both from officials and workmen. There were a total of 114 officials consulted, representing 83 foundries. Of these officials 31 admitted the presence of occupational diseases in their own plants, 26 others gave interesting statements concerning the same, 46 declared no knowledge of the same, and 11 refused any comment. Of 187 workmen, 146 reported that they were subject to brass chills.

The forms of sickness most commonly complained of were:

Brass chills, 45 of the 89 foundries.

Smoke inhalations, 26 foundries (especially fumes from oil-blast furnaces).

Other acute sicknesses, 4 foundries.

Other chronic sicknesses, 20 foundries (respiratory, gastrointestinal).

Temperature variations, 11 foundries.

Fatigue, 3 foundries.

Of the total of 2212 men and women in brass foundries it was found that 451 were engaged in processes which need not have exposed them to the foundry atmosphere. Of the remaining 1761 actually engaged in brass foundry work age statistics were carefully compiled with the following startling disclosures: 17 over fifty years of age, about 60 over forty-five years of age, and about 180 over forty years of age, leaving 1500, or 85 per cent., under forty years of age.

An investigation carried on into the zinc smelting industry in the Illinois River Valley where 3 concerns employed upward of 2000 men, disclosed the presence of the following industrial diseases and complaints: (1) "Zinc chills" which, from description by the workmen, were exactly analogous to the brass-foundryman's ague. However, this complaint was found to be of rather infrequent occurrence, as the smelters were found to be not as much exposed to the zinc smoke, as brass-moulders. (2) Lead poisoning, which was of greater frequency than among brass-moulders, because of the handling of crude ores. (3) Summer colics, which the work-

men alleged to be due to the drinking of ice-cold water when overheated, but which may have been the expression of a seasonal form of lead colic. (4) Respiratory afflictions, which existed with great frequency, and known among the men as "asthma," due to breathing zinc fumes. (5) Carbon-monoxide poisoning, among the gas-plant workers, as all of the concerns made their own gas, which was used for fuel in the smelters. (6) Industrial alcoholism, which I so name because the workmen consider alcoholic liquors antidotal to various forms of trade sickness.

LIMITATION AND PREVENTION OF OCCUPATIONAL BRASS POISONING. The chief means of preventing brass-founder's ague lie in the prophylaxis. This consists in proper hygienic arrangements in foundries and smelters, regulation of the habits of workmen, and large roomy quarters. All furnaces and furnace areas should be provided with hoods and stacks to draw off escaping vapors. In addition ceiling ventilators or skylights provided with artificial means, such as suction fans, or blower systems, to be used in inclement weather, should be provided in every furnace and foundry room. The furnace room should be separate from the balance of the foundry. In large foundries with good ventilation whether natural or artificial, brass chills practically never occur. The prevention of metallic fumes seems impracticable, although they can be largely absorbed by adding silicates, fluorides, and borate to the slag (Sigel). Adequate light, wet cleansing, and frequent whitewashing should be resorted to. In addition proper precautions as to lead poisoning in certain classes of work, as well as the prevention of the other unhygienic conditions mentioned, should be looked into.

Individual precautionary measures, such as sponges, respirators, etc., have a restricted value, but are generally little and reluctantly used. Sickly or anemic workmen, boys, and women, those with a tubercular tendency, and chronic alcoholics should not be employed in brass foundries. The workmen should not eat in foundry quarters where the air is filled with sublimation products; they should be allowed time for washing up before eating, and longer lunch periods. They should be given adequate washing facilities, and be provided with shower baths, and have suits at least of outer garments for use during work hours.

No specific treatment for brass chills has been discovered. The more careful and observing workmen use mild emetics, since they claim that the production of vomiting relieves the distressing symptoms at once, while a good purge seems as beneficial as anything. As before stated most of them resort to alcohol, usually whisky, but there is absolutely no proof that it has any beneficial effects. Many workmen seem to derive some benefit from drinking hot milk, to which they often add pepper. Sigel suggests that the workmen use sodium bicarbonate to form insoluble zinc carbo-

nate, but says that inasmuch as most (one-quarter part) of the metal finds its portal of entry by way of the respiratory system, this can do but very little good.

The State of Illinois has recently provided two laws for the effective prevention of occupational diseases, including brass poisoning, the enforcement of which lie with the Department of Factory Inspection. The first of these came in force January 1, 1910, and is entitled:

"An act to provide for the health, safety, and comfort of employees in factories, mercantile establishments, mills and workshops in this State, and to provide for the enforcement thereof."

The second came immediately following the Report of the Commission on Occupational Diseases to His Excellency Governor Charles S. Deneen, and has been enforced since July 1, 1911. It is entitled:

"An act to promote the public health, by protecting certain employees in this State from the dangers of occupational diseases, and providing for the enforcement thereof."

In certain parts of Germany, according to the statistics of Frey,³⁵ the enforcement of hygienic measures between the years 1901 and 1909 has already produced marked results in this industry.

SUMMARY. 1. In a broad sense the brass industry includes all non-ferruginous metal-working trades; zinc is invariably present to some extent; there are sixty or more common alloys (brass, bronze, German silver, type-metal, etc.). The proper physical properties are produced by combining with zinc varying proportions of other metals, as copper, tin, lead, nickel, antimony, phosphorus, etc.

2. Strictly speaking, brass is a compound of copper and zinc (lead, a trace to 7 per cent.). Bronze is a compound of copper and tin (some zinc, also lead).

3. There is no peculiar poisoning due to trauma from brass or the industrial exposure to brass dust, as among polishers, but greenish discolorations of the skin, hair, gums, etc., may occur, due entirely to the copper constituent.

4. Occupational brass poisoning or brass-founder's ague is a malaria-like complex of symptoms with certain limitations as regards occurrence, severity, susceptibility, and effects, found to occur chiefly among brass-founders, but also in all confined places where zinc is heated to the volatilization point and the resulting sublimation products inhaled.

5. This malaria-like symptom-complex is peculiar to the human being. As a rule, its severity is in proportion to the concentration of the zinc in the alloy.

³⁵ Vrtljschr. f. gerichtl. Med., Berlin, 1912, 3, F., xliii, 1, Suppl. Heft, S. 113-141.

6. There is no definite pathology, but continued exposure appears to be followed in time by chronic systemic affections (respiratory, digestive, urinary, and nervous). Zinc is found in the urine and feces.

7. The affection is very little known to physicians because it is never immediately fatal, its course is brief and self-limited and an apparent but fleeting immunity is soon established in most persons. The affection was first distinguished from malaria by Thackrah, in England, in 1830. The entire literature upon the subject to date is scarce.

8. The exact etiology is disputed. Long thought to be a copper poisoning, or an alloy poisoning, also due to other metals. Lehmann first produced the symptoms in man by burning chemically pure zinc. "Resorption of cell contents which have been destroyed or changed by zinc in the respiratory tract may be the cause of the peculiar malady."

9. Recent observations show it probable that the symptom-complex may be produced by the inhalation of the volatile products of other metals. The malady has always been associated with zinc, however, because zinc is the only supposedly innocent metal whose boiling point is commonly reached in the industries.

10. Recent perfections in the tests for zinc have enabled us to trace zinc through the lungs, liver, and kidneys of the rabbit exposed to the inhalation of brass fumes.

11. The hygienic and working conditions were investigated in 89 brass foundries and 3 large zinc smelters in Chicago and vicinity in 1910 by a State Commission, with the following findings:

(a) The large majority of these plants were without proper ventilation. Numbers of workers were also needlessly exposed to brass and zinc fumes.

(b) Workers invariably ate within the foundries, the noon hour was only thirty minutes, washing facilities were inadequate, the piece-work system prevailed (ten hours per day), and exposure to lead and its fumes, carbon-monoxide vapors and burnt oil odors were nearly universal conditions.

(c) Unskilled labor (Eastern Europeans) constituted 90 per cent. of the employees.

(d) Workmen were found in half the plants who were or had been the subjects of brass or zinc chills.

(e) About one-third of the officials consulted acknowledged the existence of these chills, but considered them of minor significance.

(f) Brass or zinc chills were far more prevalent in the winter season (natural means of ventilation curtailed).

(g) Large, well-ventilated plants or those provided with special means of artificial ventilation were seldom the site of the occurrence of these chills.

(h) Alcoholism was exceedingly prevalent, excited by chronic respiratory irritations. Undoubtedly the cause of much incapacitation. Traditionally antidotal to the effects of fumes.

(i) Trade-age-limit statistics showed: Only 17 out of 1761 men over fifty years of age and approximately 85 per cent. under forty years of age. Officials claimed workmen became too slow and undependable. Workmen claimed they were gradually incapacitated by the continued inhalation of fumes and vapors. Conditions not so among iron moulders, an analogous trade.

12. Prevention (no antidote or hardly a palliative for the zinc-chill syndrome): Restrict certain persons from the trade. Prevent the inhalation of metallic fumes as (a) by confining the fumes to certain quarters, (b) by insuring rapid ventilation, and (c) by coöperation on part of employees through instructions.

13. Following the report of the Commission the Illinois Legislature adopted a special occupational disease law effectively covering the hygiene of this and similar trades. By similar means, statistics show Germany has materially increased the trade-age-limit in this industry in recent years.

REVIEWS

THE PRINCIPLES AND PRACTICE OF OBSTETRICS. By JOSEPH B. DE LEE, A.M., M.D., Professor of Obstetrics at Northwestern University Medical School. Pp. 1028; 913 illustrations. Philadelphia: W. B. Saunders Company, 1913.

THIS text-book is a welcome addition to the field of obstetric literature. The author's twenty-one years of experience enable him to speak with authority, and the years of teaching he has spent are evident in the systematic and clear arrangement of many of the chapters. The greater part of the book is most excellent, especially the chapters on the mechanism of labor and on deformities of the pelvis. The reviewer knows of no text-book in which these two subjects are better handled. Most excellent also are the chapters on extra-uterine pregnancy; the diagnosis and differential diagnosis of pregnancy; and the greater part of the chapter on puerperal sepsis. The illustrations are superb, the publishers having exceeded even their high standard in this respect. Most noteworthy are the illustrations on the Porro Ccsarean operation, and the full-page plate, Fig. 435, of Wegner's sign of fetal syphilis.

In a book of this kind, in spite of its many good points, there are a few examples of questionable teaching; some a matter of opinion only, but some diametrically opposed to modern teaching, and also quite a few omissions of matter that should have been included. It seems strange to meet in these days an endorsement of episiotomy, based as it is on an erroneous idea of the production of perineal tears; an endorsement of the use of the finger as a curette in abortion, instead of the placental forceps; a recommendation of the use of a 1 to 1500 solution of bichloride of mercury in the vagina in labor. The chapters on toxemia of pregnancy (especially the latter half of pregnancy) are not arranged with the same care that is bestowed upon many other chapters, and the discussion of the subject is involved.

While the text recommends the use of rubber gloves, a large proportion of the illustrations omit their use, especially Figs. 312 to 318, where the technique is not such as to inspire admiration. The method of filling a colpeurynter, shown on page 456, can hardly be compared to the use of a metal piston syringe for this purpose, as the Davidson syringe shown is notoriously hard to cleanse

and care for adequately. The prohibition of disinfection of the uterine cavity in septic abortion (p. 433) is justified only when the instruments used are employed with undue force. The spread of infection spoken of is due to poor technique and not to the proper employment of either curette or placental forceps.

There are some omissions of subjects, possibly not unusual in first editions. One looks in vain, for instance, for any mention of blood pressure in eclampsia; the pulmotor or mouth-to-mouth insufflation as a means of reviving an asphyxiated child; any description or mention of cystoscopy or catheterization of ureters; any mention of extraperitoneal Cesarean section; the more modern perineal operations for repair of the injuries of childbirth, based upon an accurate knowledge of the site and character of the injuries. The chapter on abnormalities of the newborn child might with advantage be made more comprehensive in future editions. Much too little is said of the consequences of childbirth, to be managed during the puerperium or shortly afterward; in this respect the book does not follow the proper course of safeguarding the patient's future comfort, but deals with the subject from the standpoint of midwifery rather than obstetrics.

These criticisms are mostly of a minor nature, however. The book is a valuable one, and worthy of a place of honor in any medical library.

The make-up of the book and particularly the illustrations are on the very highest plane.

J. C. H.

A TEXT-BOOK ON THE PRACTICE OF GYNECOLOGY. FOR PRACTITIONERS AND STUDENTS. By W. ESTERLY ASHTON, M.D., LL.D., Professor of Gynecology in the Medico-Chirurgical College of Philadelphia. Fifth edition. Pp. 1100; 1050 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

THE general arrangement as well as the subject matter of this last edition differs but little from that of former editions so well known to the profession. Throughout, the book is characterized by minuteness of detail in both description and illustration which in the author's opinion, is essential to a book intended primarily for the general practitioner and student. While much can be said in favor of this plan, we believe that such efforts have been carried too far thus detracting from rather than contributing to the object in view. The student as well as the practitioner seeks essentials elaborated by detail only when the importance of the subject demands further elucidation. The schematic drawings

are as a whole good, but here again the idea of detail runs rampant and many illustrations could be omitted with benefit. For example, we cannot see the necessity of depicting the instruments required for each operation or such well-known articles as a glass rod, an alcohol lamp, a rubber glove, etc. This fault detracts from what is otherwise an excellent book, in which a large practical experience has been the guiding hand in presenting the modern views of gynecologic diagnosis and treatment. The various aspects of each disease are exhaustively discussed and the treatment advised is characterized by sound conservatism and good judgment. In this last edition such alterations and additions have been made as were necessary to bring the work up to date. The use of the x-rays in the treatment of uterine myomas is briefly mentioned and is recommended in only exceptional cases. Fulguration is advised as a routine treatment in operations for cancer and desiccation advocated in the treatment of warty growths of the vulva. Minor changes have been made in the chapter dealing with cystitis; cystoscopy is described but the entire chapter is antiquated and should be rewritten. The von Pirquet test is recommended in the diagnosis of tuberculosis; the more important focal reaction following the subcutaneous injection of tuberculin is not mentioned. Additions to pathology include actinomycosis, malignant leiomyoma, Krukenberg's tumor, pseudomucinous cystadenoma, and the investigations of Loeb concerning the etiology of dermoid cysts. The treatment of gonorrheal and septic infections of the uterus and tubes has been practically rewritten and conforms with the views now generally accepted. Changes in technique and operations include the use of iodine in the preparation of the field of operation, Baldy's suspension of the uterus, Ward's treatment of vesicovaginal fistula, salpingo-oöphorectomy and partial hysterectomy, and the author's recently adopted method of removing the appendix.

F. E. K.

THE PARASITIC AMEBÆ OF MAN. By CHARLES F. CRAIG, M.D., Captain, Medical Corps, United States Army. Pp. 253; 30 illustrations. Philadelphia and London: J. B. Lippincott Company.

THE importance of the subject to the medical profession amply justifies the publication of Captain Craig's monograph as a presentation of an authoritative review of the information which has thus far been acquired of the amebæ parasitic in man with exposition of proved methods of study for their recognition and identification. The book includes chapters upon the history of this subdivi-

sion of microbiology, on the morphology and biology of amebæ in general, upon their classification, the technique of the study of parasitic species, the question of the possibility of their artificial cultivation, with systematic description of those parasitic forms to be met in the human intestinal tract, in the mouth, the genito-urinary tract, and in exudates, abscesses, and in the lungs.

It is true that the book might without loss be materially condensed, and suffers somewhat from unnecessary repetitions and diffuseness of the discussions; but at the same time it is written in an easy conversational style which cannot be without attraction for the reader, and the material presented and in general, the opinions stated are altogether commendable. The chapter on technique is a timely one and valuable to any medical man desiring to pursue study along the author's lines; and the descriptions of amebic parasites with the points emphasized for the study of the different species are reliable. Naturally differences of opinion exist in these matters as in most others, but the reviewer feels that Craig has been frank and fair in setting forth his position upon such moot points, as for example, the question whether the cultivation of pathogenic amebæ has actually been accomplished, as by Musgrave and Clegg, or whether the forms obtained in culture are not really independent types. Craig follows the usage of the best protozoölogists in his nomenclature; employing the generic name *entameba* proposed by Casagrandi and Barbagallo in 1897 for parasitic amebæ (*Annali d'Igenie Sperimentale*, vii, 103). However, in 1879 Leidy (*Proc. Acad. Nat. Sci.*, Philadelphia, xxxi, 204) proposed the generic name *endameba* for parasitic amebæ, dealing at the time with a parasitic ameba of the cockroach; and, therefore, by our modern rules of nomenclature the name should be spelled with a "d" instead of a "t," with attachment of Leidy's name instead of those of Casagrandi and Barbagallo when reference to the genus alone is made. The writer is in full accord with the author in questioning the validity of a number of species which have been proposed, as *Endameba kartulisi*, *E. pulmonalis*, *E. nipponica*, *E. urogenitalis*, and others. As a matter of personal interest he would have been pleased to have noted discussion by Captain Craig of the *E. mortinatalium* presented in 1910 by Smith and Weidman in minute abscesses in the kidneys and elsewhere in a stillborn infant. One misses in the work any reference to *Leydenia gemmipara*, Schaudinn, which because of its discovery in connection with cancer was for a time a matter of wide interest and is commonly included among the protozoan parasites of man; but he is technically correct in excluding it from the limitations set to the present volume since it is now known to be in reality only an amebiform stage of one of the Foramenifera, *chlamidophrys stercorsa*, Cienkowski. Nevertheless, from a comparative standpoint, for purpose of enabling differentiation in case of occurrence,

it might well have been given appropriate space. Suggested by analogy, some question might be raised in the matter of classification in case of the author's *Parameba hominis*, fully and in the reviewer's opinion very properly presented. It should be remembered that Schaudinn's genus *Parameba* is by no means above doubt as to its precise relation, the amebic stage being succeeded by a flagellate form bearing two chromatophores in the type species *P. eilhardi*, Schaudinn. There is a chance that an ameba and a flagellate have here been confused; or perhaps the prominence in classification should be given rather to the flagellate phase than the amebic. These, however, are all matters which in no sense detract from the real value of Dr. Craig's book to medical men; and at best are for the most part open to personal interpretation. The volume is a valuable contribution to English-speaking medical men, and should be accorded warm appreciation.

A. J. S.

VORLESUNGEN ÜBER KLINISCHE HEMATOLOGIE. By DR. WILHELM TÜRK, Privatdozent für innere Medizin an der Universität in Wien. Part II, first half. Pp. 410. Vienna and Leipzig: Wilhelm Braumüller, 1912.

THE author explains in the preface that the reason for the delay in the appearance of this the second part of his "Vorlesungen" is largely due to the fact of his withdrawal from the Neusser clinic and the assumption of manifold new duties at the Kaiser Franz Joseph Hospital. In a certain sense this first half of the second part, in conjunction with Part I, should constitute Volume I of the entire book as it is planned. Part I covered much of the general pathology and anatomy of the blood, and in the present division of the work there are taken up particularly the physiology of blood formation, the biology and functions of the cellular elements of the blood, leukocytic reactions, including eosinophilia and the mast-cell reactions, inflammation, and variations in blood picture due to physiological conditions and alterations of environment.

There is in press a second half of the second part, which takes up the anemias and polycythemias, as well as the pathology of the erythroblastic apparatus; this is to be regarded as Volume II of the entire work.

The third part will cover the leukemias, the leukocytic reactions of infections, and the pathology of the leukoblastic apparatus. The plates for this volume are complete, but the text is not yet written.

The volume under discussion is an excellently arranged and

philosophical discussion of the various topics indicated above. Controversial matter is given brief consideration, and the writer's authoritative views given clearly and concisely. Embryology and morphology are considered in the usual way, but the work is made interesting by the discussion of the function of the various cells and cell groups under both normal and pathological conditions. If the reader seeks for immediately practical points in this book he will be disappointed, but if he seeks for enlightenment as to the broader significance of the function of blood cells and of their various changes in form and number he will be entertained and instructed by almost every paragraph. The book contains little that is original that has not appeared in monographs and other publications, but it is up to date in every particular.

H. T. K.

IMMUNITY. By JULIUS CITRON, M.D., Assistant at the University Clinic of Berlin, Medical Division. Translated from the German and edited by A. L. GARBAT, M.D., Assistant Pathologist, German Hospital, New York. Pp. 209, 27 illustrations, 2 colored plates, and 8 charts. Philadelphia: P. Blakiston's and Co., 1912.

GARBAT has presented with some additions an English translation of a work well known in Germany, the author of which, by reason of his extensive research and wide experience as a teacher, has treated his field with fulness and precision. Citron's manual on *Immunity* is at once a hand-book for the laboratory worker, and on account of its illuminating discussion of principles, a reference work for the clinician.

The book is so arranged that the physician even slightly familiar with the methods of the laboratory may learn the details of the various reactions and their significance. Methods which are used for diagnostic, therapeutic, and prophylactic purposes are discussed. There are also included fundamental considerations of immunity problems from a theoretical standpoint.

As a text-book, Citron's work is orderly and the text clear. The results of the various methods are presented critically. The beginning of the book is occupied with a discussion of the principles underlying immunity problems and a detailed description of laboratory technique. Then follows an account of active immunity with details of vaccination against small-pox, rabies, and typhoid fever. A large portion of the book is devoted to the important subjects of immunity against tuberculosis and syphilis, the account of the nature of the immunity acquired after tuberculin injections being of particular interest. It is rather astonishing to observe

that the author regards the ophthalmoreaction with so much favor.

The subjects of toxins, agglutinins, precipitins, bacteriolysins, and hemolysins are duly considered in accordance with the present state of knowledge regarding them. The discussion of toxins includes those derived from the higher plants and animals as well as from bacteria. The translator has somewhat revised the chapter on vaccines, and elaborated it to conform more closely to the most recently advocated views of Sir A. E. Wright. It is interesting to read that Wright does not insist so strongly as formerly on the determination of the opsonic index during vaccine treatment, and that Matthews, one of his assistants, states that in many cases, such determination is quite out of the question.

The consideration of immunity against the meningococcus seems brief, in view of the importance of the subject. Anaphylaxis too is little more than mentioned. The illustrations are adequate, the colored plates most excellent, and the experiments cited are accompanied by elaborate protocols.

H. G. S.

DIAGNOSTIC METHODS. By RALPH W. WEBSTER, M.D., PH.D.,
Director of the Chicago Clinical Laboratory. Second Edition.
Pp. 682; 37 Colored Plates and 164 Other Illustrations. Phila-
delphia: P. Blakiston's Son & Co., 1912.

THE second edition of Webster's *Diagnostic Methods* is an admirable hand-book for the laboratory, remarkable for its thoroughgoing character and conciseness. The selection of methods is wide and their description clear, the author emphasizing always the fact that laboratory results can be properly interpreted only in their relation to clinical phenomena. Much has been rewritten since the first edition, certain features eliminated, and many recent laboratory researches of proved value added. Among the latter may be noted the antiformin method for tubercle bacilli; Neubauer and Fischer's glycol-tryptophan reaction; Kendall and Day's method for isolating typhoid bacilli from the feces; Benedict and Bang's tests for glucose in urine; Wright and Kinnicut's method of counting the blood plates; Folin's newer methods for urinary sulphur compounds; the formalin method for ammonia in urine; colloidal nitrogen; the phenol sulphonephthalein test for functional activity of the kidneys; Noguchi's method for cultivating the spirochæta pallida; the tuberculin and luetin reactions; Noguchi's butyric acid test. The Wassermann reaction with its modifications is treated at length, and the section on serum pathology has been considerably enlarged. The book is well printed, of convenient size, and the numerous illustrations and plates are adequate.

H. G. S.

COMPENDIUM OF DISEASES OF THE SKIN. By L. DUNCAN BULKLEY, A.M., M.D., Physician to the New York Skin and Cancer Hospital, etc. Fifth Edition, Pp. 286. New York, Paul B. Hoeber, 1912.

THE last edition of the writer's work appeared twelve years ago, and the present volume is of practically the same size and, with a few exceptions, of almost the same contents. The work consists of the subject matter contained in a course of lectures given by the writer at the New York Hospital. The rarer diseases have not been added, as the book is intended simply as an introduction to the subject of dermatology and for the general practitioner. Thirty thousand cases of diseases of the skin are reviewed by the writer, and there is also a therapeutic formulary. The work would be of greater value if more new material had been added, and if a certain remedy mentioned in the treatment of epithelioma, had been omitted.

F. C. K.

PSYCHOLOGICAL MEDICINE. By MAURICE CRAIG, M.D. Second edition. Pp. 474; 17 plates. Philadelphia: P. Blakiston's Son & Co., 1912.

CRAIG in this book successfully attempts to treat the subject of insanity in a way particularly adapted to the teaching of students and general practitioners. His work contains considerable research of his own and many points of value and interest to an alienist. The author's lucidity and conciseness are most commendable.

The first part of the book takes up, in a manner as brief as clearness will permit, the study of normal psychology. Here sensation, affection, attention, conation, and other kindred subjects are considered.

The discussion of the term insanity and the etiology are next treated. The effect of metabolic changes is discussed, with the bacteriological and serological findings and conclusions of Bruce and others. Then, following a chapter on classification, comes symptomatology, a well-arranged and most useful section of the book. The diagnosis of beginning forms of insanity is here urged as most important, and the symptoms so often occurring as forerunners of insanity are taken up in considerable detail. Original investigations on blood pressure and metabolism are given with some of other authors.

In the chapters on mania and melancholia the so-called acute maniacal delirium described by Branchi and Piccinino is mentioned, and further original investigations are described. More than usual

stress is given to the danger of suicide in melancholia, a most important point which cannot be too strongly impressed.

The consideration of forms of stupor (anergic, post-melancholic, post-maniacal, catatonic), paranoia, and dementia præcox, is very thorough, and in the chapter on puerperal insanities an interesting opinion is given as to the probable effect of pressure upon the splanchnic vessels during pregnancy, causing high blood pressure and melancholia, whereas the fall in pressure after childbirth might account for the greater frequency of the maniacal outbreaks during this period.

Following the chapter on intoxication psychoses, paresis, the most important perhaps of all mental diseases, is discussed in a particularly thorough and detailed manner. Many original suggestions are advanced, among which is the author's belief that anti-syphilitic treatment is contraindicated in tabes and paresis, but that all measures should be used to reduce the possibility of cellular changes from exhaustion.

Dr. Craig emphasizes the impossibility of syphilis alone causing paresis, and he also suggests the possibility of the different types of paresis being dependent upon the type of brain tissue primarily involved.

Of the remaining chapters, all of which are written in accord with the standard of the earlier chapters, the ones dealing with epileptic insanity and feigned insanity and treatment are the most important, and corresponding weight is given to their discussion.

Throughout the work any points of medicolegal interest are clearly shown, and in a chapter devoted to the legal aspect of insanity, allowance must be made for the differences in the English and American codes. Many valuable plates (plain and colored), are given, including gross cortical changes and microscopic cellular degenerations in different diseases.

E. M. W.

GYNECOLOGICAL NURSING. By ARTHUR E. GILES, M.D., B.Sc., F.R.C.S., M.R.C.P., Surgeon to the Chelsea Hospital for Women, Gynecologist to the Prince of Wales' General Hospital, Tottenham. Pp. 182; 41 illustrations. New York: William Wood & Co., 1912.

FROM cover to cover this little book contains a mine of information, couched in simple, readable diction. The introduction gives the author's conception of an ideal gynecological nurse, and it would be well for every nurse to learn it by heart as an important part of her stock in trade. The first three chapters are devoted to the anatomy, physiology, and diseases of the pelvic organs; the

author has selected the important points under each heading and describes them in such a manner as to make them thoroughly understandable. No detail is spared in the chapters dealing with the preparation for operation and the conduct of the nurse during the operation; every possible contingency is met, including the sterilization of instruments, suture materials and accessories, preparation of the room in hospital or private house, and the preparation of the patient before and during the operation. Post-operative treatment is likewise fully described, together with the commoner complications, their danger signals and treatment. The book is good throughout, and will prove of great value not only to the nurse for whom it is intended, but also to those who undertake the instruction of nurses in this branch of surgery. F. E. K.

THE PREVENTION OF DENTAL CARIES. By J. SIM WALLACE, D.Sc., M.D., L.D.S. Dental Surgeon and Lecturer on Dental Surgery and Pathology, London Hospital; Honorary Dental Surgeon to the West End Hospital for Nervous Diseases. Second edition. Pp. 70. London: Dental Record, 1912.

In this small volume the author sums up his views of the etiology, pathology, and prevention of dental caries. He says that "the cause of dental caries is the prolonged retention or stagnation of fermentable carbohydrates in more or less immediate contact with the teeth and undisturbed by the free access of saliva." He claims that the only reliable method of preventing dental caries is the natural or physiological one, *i. e.*, self-cleansing of the mouth by foods that do not lodge between the teeth. In his opinion this is far more important than artificial procedures by tooth-brush, powders, and mouth washes, which have principally a cosmetic rather than a hygienic value.

If the book were read and its principles followed out by every physician, dentist, and layman having the care of children's teeth, the incidence of dental caries would be enormously reduced.

R. H. I.

SALBEN UND PASTEN MIT BESONDERER BERÜCKSICHTIGUNG DES MITIN. By DR. S. JESSNER, Sanitätsrat. Second edition; pp. 39. Würzburg: Curt Kabitzsch.

THE author first discusses the advantages and the disadvantages of the various salve bases, the absorptive properties, the ease with

which they may be applied, and the indications for the application of the same. Adipis, vaselin, paraffin ointment, vasogenum spissum, esypus, and casein ointment being among those mentioned. Casein ointment consists of cheese, water, and vaseline. Benzoated lard has the advantage over the plain lard of not becoming rancid. Various pastes are suggested as useful; chief stress is laid on the paste of Lassar, consisting of zinc oxide, starch, and vaseline, and Unna's paste, made of zinc oxide, terra silicea, and benzoated lard. The author has suggested the name "Mitin" for a base of his own composition which has an unusual faculty of absorption. The base consists of cold cream, resorbin, and eucerin. Resorbin consists of a fat, oil, and water; gelatin holding the ingredients together. Eucerin is a paraffin ointment. The base is of a thin or thicker consistency, depending upon the proportion of these substances combined. By combining powdered zinc oxide, starch, etc., to the base a white paste may be obtained. Various formulæ are given in the appendix showing drugs made up with Mitin as the base. F. C. K.

CARBONIC-ACID SNOW AS A THERAPEUTIC AGENT IN THE TREATMENT OF THE DISEASES OF THE SKIN. By R. CRANSTON LOW, M.B., F.R.C.P.; Assistant Physician to the Skin Department, Royal Infirmary, Edinburgh. Pp. 117; 16 illustrations. New York: William Wood & Co..

Low has contributed a small volume which is not only of interest to the dermatologist, but also to all those practitioners of medicine who are interested in the newer therapeutic measures. The various methods for the collection and the moulding of the carbonic-acid snow are described in detail. The amount of pressure required and the duration of the application of the moulded snow are thoroughly and practically considered. A very interesting chapter gives the microscopic picture of the skin some hours and also some days after the application of the snow; the histological appearance explaining the action of the therapeutic agent. The results obtained in the treatment of numerous diseases of the skin are recounted. The most favorable response having been noted in nevus vascularis, nevus pigmentosus, and lupus erythematosus. The ninety-four references quoted make the volume of particular value to those using this method of treatment. F. C. K.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Treatment of Leukemia with Benzol.—A. v. KORÁNYI (*Berlin. klin. Woch.*, 1912, xlix, 1357) has tried benzol in the treatment of leukemia. He was led to do this by the results of experimental studies published by Selling, who showed that in animals poisoned with benzol, after a transitory rise, the leukocytes gradually decrease in number, and finally disappeared entirely from the blood, whereas the number of red blood cells underwent only a moderate decrease. Selling also observed a marked aplasia of the bone marrow, spleen, and lymphatic tissues in general. After withdrawal of the benzol, regeneration took place. Having a number of leukemias in the clinic, Korányi determined to use benzol in treating them. His experiences with it he summarizes as follows: (1) After a temporary increase in the number of white blood corpuscles, benzol causes a marked improvement in the leukemic blood picture. The decrease in number of the leukocytes begins usually at the end of the second or the beginning of the third week, proceeding slowly at first, then more rapidly. After a slight initial decrease, the number of the erythrocytes remains practically constant; after prolonged treatment, he has even noted an increase in the number of red cells. This sequence of events appears to occur in all forms of chronic leukemia. The spleen decreases in size, but the lymphatic glands are less influenced. The general condition of the patient improves much as it does with successful Röntgen treatment. (2) Benzol produces improvement less rapidly than the x -rays, but it may benefit a patient who fails to respond to the latter. Patients who have been treated previously with the x -rays seem to respond to benzol more promptly than others. The effect of the benzol

treatment is not lasting. (3) Small doses of benzol seem to stimulate leukopoiesis. Therefore, large doses are indicated in leukemia. Three to 4 grams of benzol daily may be borne for months. In certain cases Korányi has given 5 grams for short periods of time, but unpleasant effects, such as burning in the stomach, eructation, short attacks of tracheobronchitis, and vertigo, may follow. Gastric disturbances are usually lacking if equal quantities of oil are placed in the gelatin capsules with the benzol. If vertigo is complained of, the dose should be lessened. (4) Korányi has also used benzol in a patient with polycythemia and splenic tumor. The result was encouraging. At the end of the first week of benzol treatment, the number of erythrocytes rose from 9,000,000 to 10,000,000, but in the next three weeks it fell to 6,700,000. As the patient considered himself cured, he disappeared from observation. It will require more extended observations to determine the value of benzol in the treatment of leukemia and erythremia, but it seems worthy of thorough trial.

The Carbon Dioxide Tension in the Alveolar Air in Acute Febrile Disease.—L. S. FREDERICIA and O. OLSEN (*Deutsch. Arch.f. klin. Med.*, 1912, evii, 236) have investigated the carbon dioxide tension in the alveolar air in acute fevers. It has been shown that the carbon dioxide tension is lowered in conditions where the oxygen supply is lessened, after excessive bodily exertion, in cyanotic cardiac patients, in diabetes in coma or with untreated acidosis, and in uremia. The studies of Fredericia and Olsen show that in patients with acute febrile diseases the carbon dioxide tension of the alveolar air is also frequently lowered. They consider it possible that this is due to the mild acidosis which is frequently associated with febrile disorders.

A Test of Pancreatic Function.—R. EHLMANN (*Berlin. klin. Woch.*, 1912, xlix, 1363) describes a new, simple test of pancreatic function. It is based on the fact that neutral fat free from fatty acid is split only by pancreatic lipase; the resulting fatty acids are then converted into their green eupric salts. Commercial palmin has proved to be the most suitable neutral fat. Other fats, such as butter and oils, cannot be used. Emulsified fat in the form of milk or cream is also unsuitable, since it may be hydrolyzed by ferments other than pancreatic, although the butyric acid odor noted after removal of these foods from the stomach is due chiefly to the action of pancreatic enzyme. The patient takes the following test breakfast on the fasting stomach: About 30 grams of ordinary rice starch are dissolved in about one-fourth of a liter of water, and warmed somewhat. In this solution about 57 grams of palmin are stirred; the palmin is melted by warming. The mixture is drunk from a glass, and is allowed to remain in the stomach two to two and one-half hours, when it is removed. In testing the gastric contents, two solutions are required: Solution I, petroleum ether, 90, benzol to 100; Solution II, eupric acetate, 3, distilled water to 100. A portion of the fatty gastric contents is shaken vigorously with an equal quantity of solution I. The ether layer, after separation, is poured into a second test-tube, and is then shaken with an equal volume of solution II. The ether which again separates is stained more or less intensely emerald green, depending

upon the concentration of fatty acids in the gastric contents. With no hydrolysis of the palmin, the ether remains water clear. If the gastric contents are very acid (Congo paper turned a very dark blue), the reaction may be weak or may fail even with normal pancreatic secretion. In such case, repeat the test breakfast, adding to it a teaspoonful of sodium bicarbonate.

Contributions to the Pathology and Therapy of Very Severe Cases of Diabetes Mellitus.—R. GRAFE and CH. G. L. WOLF (*Deutsch. Arch. f. klin. Med.*, 1912, cvii, 201) have made complete metabolic studies of 3 very severe cases of diabetes mellitus. (The details of their studies cannot be adequately reviewed; the original must be consulted.) They have determined quantitatively the sugar, total nitrogen, acetone, β -oxybutyric acid, creatin, and creatinin, ammonia, "formol," and colloidal nitrogen, and have made observations upon the respiratory exchange of gases in the lungs. In 2 of the patients the acetone excreted was extraordinarily high. The dextrose-nitrogen ratio exceeded 5 over long periods of time, so that formation of sugar from fat must be assumed. They also found the respiratory quotient high in the same 2 patients. This apparent contradiction has also been found by other observers. From comparison of the analyses of the respiratory experiments and of the urine voided at the same time, Grafe and Wolf conclude that the dextrose-nitrogen value and the respiratory quotient may be harmonized only if one assumes either that, twelve to eighteen hours after a rich carbohydrate meal, the severe diabetic possesses at least 20 grams of glycogen for oxidation or synthesis, or that a still unknown anomaly of metabolism is at play. Since there are no grounds to support the latter view, the first supposition is assumed to be correct. The relation of the creatin excretion furnishes a valuable index of the character of a case of diabetes; the more severe the case, the greater is the quantity of creatin excreted. Therapeutically, Grafe and Wolf found very large quantities of alcohol (equivalent to 100 to 160 grams of absolute alcohol daily), and large doses of alkali (sodium bicarbonate and sodium citrate, 70 to 100 grams daily for weeks) very useful. The beneficial effect of the alcohol was seen not only its action upon the acidosis, but also upon the sugar excretion.

A New Test for Diacetic Acid in the Urine.—B. V. ONDREJOVICH (*Deutsch. med. Woch.*, 1912, xxxviii, 1413) reports a modification of Lindemann's reaction for diacetic acid. Method: To 5 c.c. of urine add 5 drops of 50 per cent. acetic acid. To this mixture add a 0.2 per cent. methylene blue solution until the whole assumes a marked blue color; usually one drop suffices. Four drops of tincture of iodine are now placed in this mixture, on which the color changes to red. If diacetic acid is present, the blue or green color returns within one minute at the most; otherwise, the red color persists. The reaction depends upon the fact that in acid solution diacetic acid binds the free iodine, forming a colorless compound. Normal urine is supersaturated with free iodine after the addition of 4 drops of the tincture to 5 c.c. of urine; the excess of iodine unites with the methylene blue to form a red compound. An excess of acetic acid is to be avoided.

Ondrejovieh finds the reaction twice as delicate as the Gerhardt test. If the urine contains so much diacetic acid that the reaction between it and iodine is instantaneous, the blue color remains unaltered. No substances have been encountered in the urine which interferes with the reaction.

Salvarsan in Chorea Minor.—J. SALINGER (*Münch. med. Woch.*, 1912, lix, 1376) adds another to the small list of cases of chorea minor which have been treated successfully with salvarsan. The patient, a girl, aged ten years, suffered from hereditary lues and chorea. The involuntary movements of the extremities were so violent that she was unable to write and frequently fell when attempting to walk; she constantly made grimaces. The Wassermann reaction was positive in the patient as well as in her father. Because of the lues, the patient was given 0.1 gram salvarsan intravenously. The same evening the involuntary movements had practically ceased. That the rapid improvement was not attributable to the more favorable surroundings of the hospital ward is probable from the fact that the patient, after a stay of two days, was discharged and remained well at home. In spite of the good results obtained in this case, in which lues also existed, Salinger believes that salvarsan should be used cautiously and not indiscriminately in chorea.

Scarlet Red in Artificially Produced Gastric Ulcer.—With the idea that scarlet red might have a beneficial effect in gastric ulcer similar to that observed following its use in the treatment of ulcers of the skin, DAVIS and DENNING (*Johns Hopkins Hosp. Bull.*, 1912, xxiii, 332) conducted a series of canine experiments studying the effect of the dye on artificially produced gastric ulcers. In a series of preliminary experiments they demonstrated the non-toxicity of the drug when taken internally, and noticed also that it had no purgative effect, nor did it affect the action of the kidneys. It was found, however, that the dye is a fat selecting vital strain being gradually eliminated in the course of months. Ulcers of varying depths were produced by means of a special punch. In one series of dogs the drug was given in 1 per cent. solution in olive oil in doses of 10 to 20 c.c., the total amount varying between 70 and 150 c.c. Five animals were thus treated and later sacrificed. Four showed more advanced healing of the ulcers than in the controls, and in the fifth both feeder and control were equally advanced toward healing. A second set of animals, fed with olive oil alone, revealed at autopsy ulcers which in 4 out of 5 cases showed less epithelial stimulation than in the corresponding experiments in which scarlet red olive oil was used. In these instances these ulcers were farther advanced toward healing than the controls, in one equally advanced, and in another less advanced. In the corresponding experiments in which scarlet red olive oil was used. In these instances these ulcers were farther advanced toward healing than the controls; in one equally advanced, and in another less advanced. In conclusion, Davis and Denning feel that the scarlet red solution caused a more rapid and better developed growth of epithelium in the group in which it was used than in the duplicate group in which olive oil alone was administered. The results with dry powder were not

favorable experimentally, but this may have been due to the fact that the material was not continuously in contact with the denuded area.

Eosinophiles in the Urine in Bronchial Asthma.—A. EDELMANN and L. KARPEL (*Deutsch. med. Woch.*, 1912, xxxviii, 1271) report their study of the urine of 4 patients suffering with bronchial asthma. In all of the patients there was noticed a slight cloudiness of the urine following the attacks of asthma, so that a cystitis was suspected at first, though there were no symptoms to suggest such a condition. The fresh specimen of sediment showed many leukocytes. Stained preparations revealed an eosinophilia of as much as 30 per cent. Careful examinations then showed that eosinophiles were always abundant in the urine following the asthmatic paroxysm. In none of the patients were there symptoms referable to the genito-urinary tract, and no epithelial cells or bacteria were found in the urine. There was no gonorrheal infection. The urinary changes consisted in the appearance of leukocytes alone; no other formed elements, such as casts or red blood cells, were found. The number of leukocytes resembled that seen in cystitis. There was no albuminuria. The cells make their appearance in the urine, as stated above, just after the paroxysm; during the dyspneic period the urine is clear or contains only an occasional leukocyte. The cells persist in the urine from a few hours to two days. Differential count of the cells of the urinary sediment showed 30 per cent. of eosinophiles in a patient whose blood contained only 8.5 per cent. of these cells. Edelmann and Karpel describe their methods of staining the cells of the sediment.

Lymphocytosis in Diabetes Mellitus.—L. CARO (*Berlin. klin. Woch.*, 1912, xlix, 1514), who called attention to the lymphocytosis of Basedow's disease in 1907, now reports the examination of the blood of 28 diabetics—a phase of the disease which has apparently been neglected heretofore. Practically all cases showed a reduction in the number of erythrocytes and in percentage of hemoglobin. The leukocytes were normal in number. Of the 28 cases, 22 exhibited a marked lymphocytosis; in 15 of the cases the lymphocytes varied between 40 and 70 per cent., while 7 cases showed less than 40 per cent. Only 6 patients had a normal percentage of lymphocytes (or a slight increase), but in these there were complications, such as suppuration, gangrene, tuberculosis, bronchiectasis. In 8 instances the eosinophiles were increased (up to 500 cells per cmm.). The lymphocytosis is independent of the severity of the disease and of the sugar content of the urine. No interpretation of the lymphocytosis is attempted. The thyroid gland is apparently not concerned in its production.

The Diagnostic Value of the Coin Sound in Pleuritic Effusions.—B. M. SLATOWERCHOWNIKOW (*Deutsch. med. Woch.*, 1912, xxxviii, 1282) has studied the *signe du sou*, described by Pitres in 1898, in 48 cases, 28 of which were exudative pleuritis. He finds that the most satisfactory method of eliciting the phenomenon is to have an assistant tap with one coin upon another which is placed over the dull area.

while the examiner auscultates the opposite side of the chest. If spongy or alveolar tissue intervenes between the points of percussion and auscultation, a dull tone without metallic quality is heard. With an air space (pneumothorax) the tone is, of course, intensely metallic. If a solid tissue or fluid is interposed between the points of percussion and auscultation, the sound is transmitted with an appreciable metallic quality. Heterogeneous tissue, as alveolar tissue and fluid, causes the sound to be simply dull. It is evident, therefore, that the distribution of the 'metallic sound in pleural effusion should correspond with the areas of dulness and diminished vocal fremitus. Slatower-chownikow finds, however, that the *signe du sou* extends 1 to 1.5 cm. beyond the lines marked out by percussion and vocal fremitus. With the exploratory needle he was able to demonstrate that fluid extended to the line given by the coin sound. He finds this method of examination very helpful in patients with weak voice. It is doubtless because of the difficulty of examining vocal fremitus in children that Pitres' observations have found their widest acceptance among pediatricians.

The Pathogenesis of Purpura Hæmorrhagica with Especial Reference to the Part Played by the Blood-platelets.—DUKE (*Arch. Int. Med.*, 1912, x, 445) réemphasizes the fact that in studying the various hemorrhagic diseases one must investigate all the various factors involved—bleeding time, coagulation time, platelet count, fibrinogen content, etc. The particular group of cases under consideration present a characteristic clinical picture: Purpura (petechia or ecchymoses), a tendency to bleed from every vascular lesion no matter how produced (prolonged bleeding time), normal coagulation time, a firm blood clot, and a clot which does not retract and exude serum. In milder cases the same essential condition may manifest itself only by ecchymosis, following slight injury, epistaxis, or hemorrhage due to local cause such as intestinal ulcers, esophageal varices, or profuse and prolonged menstruation. Coagulation time is always normal, the clot firm, retractility diminished. These conditions Duke believes to be due wholly or in part to the enormous reduction in the number of blood platelets which he found invariably present. In 7 severe cases showing the picture described above the number of platelets was reduced almost to the point of absence, all the counts being below 10,000, and as a rule below 1000 (normal, 200,000 to 400,000). In 6 milder cases they varied from 20,000 to 65,000. It was observed that the symptoms of the disease ran a course roughly parallel to the number of platelets, appearing when they fell to a very low level, and disappearing when the count rose. Furthermore, in 2 cases there was immediate relief following direct blood transfusion, and the relief being coincident with the increase in platelets following the transfusions. In both the clinical cases and in animals in which the platelet count was changed with subcutaneous injections of benzol, diphtheria toxin, and tuberculin, it was found that extreme symptoms of purpura hæmorrhagica only appeared when there were very low counts. Several counts of 40,000 to 75,000 were observed in patients who had no marked tendency to bleed, but no counts lower than these were observed in patients not subject to hemorrhage. Finally Duke points

out that this symptom complex may complicate various diseases, such as lymphatic leukemia, hemorrhagic smallpox, tuberculosis, nephritis, benzol poisoning, aplastic anemia, and diphtheria; the one feature in common being the low platelet count, and the resulting absence of contractility of the clot. Purpura hemorrhagica of the type described would seem, therefore, to be a symptom and not a disease.

Rhythmic Contraction of Heart-muscle Cells in Culture Media.—Using his adaptation of Harrison's cultural method, M. T. BURROWS (*Münch. med. Woch.*, 1912, lix, 1473) finds that the heart muscle cells of the chick embryo, after they have undergone division and differentiation without the organism, again assume their specific function both as isolated cells and as masses of cells. The rhythmic contraction of such cells corresponds to that of the heart of the living animal. The rhythmic movement was observed not only in the heart-muscle cells of young embryos, but also in the cells of embryos fourteen days old. Parts of the ventricle which are obtained from the older embryos do not themselves contract, although the isolated cells which have wandered out from such masses beat rhythmically. These observations furnish direct evidence in support of the myogenic theory of the heart beat.

SURGERY

UNDER THE CHARGE OF

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Tubercle Bacilli in the Circulating Blood in Surgical Tuberculosis.—KRABBE (*Deut. Zeitschr. f. Chir.*, 1913, cxx, 370) examined 30 cases of surgical tuberculosis for the purpose of determining the value of the blood examination in differential diagnosis. Of 18 bone cases which were determined clinically to be surely tuberculous, the findings were positive in 12 or 66.6 per cent. Five cases of lymph node tuberculosis gave only one positive result, or 20 per cent. Four cases of skin, mucous membrane and tendon sheath tuberculosis, gave only one positive result, or 25 per cent. When we assume that a tuberculous infection of the lymph nodes is the result, in most cases, of a direct infection from the mucous membrane of the mouth or the tonsils, and as in skin diseases, it is a local process, it is easy to understand that the bacilli as a rule do not get into the blood. On the other hand, for the occurrence of a bone or joint tuberculosis, it is necessary for the

tuberculous material to first find its way into the circulation and then to be deposited at a site of lessened resistance. This explains why the tubercle bacilli can be found so frequently in these cases. The age of the patient and the duration of the process have little to do with the frequency with which the bacilli are found in the blood, and the finding of them has little to do with the question of the prognosis. The most important question that can be raised is as to whether the presence or absence of the bacilli can aid in the differential diagnosis. In one of Krabbel's cases the positive findings of the bacilli made the diagnosis certain before the histological examination of a specimen obtained at the operation furnished proof of the tuberculous nature of the condition. Krabbel believes that in cases in which there is not yet a clinically demonstrable lung tuberculosis, to point to a bacillemia, the positive findings of the bacilli can be of great importance in making the diagnosis certain.

A Contribution to the Anatomy and Pathology of Striped Muscle Fibers. Experimental Studies on the Theories Concerning Muscle Paralysis and Contracture.—KROH (*Deut. Zeitschr. f. Chir.*, 1913, cxx, 302 and 471) undertook an experimental study of ischemic muscle changes, being stimulated by the previous work of his chief, Bardenheuer, on the same condition. Ischemic contracture is a chronic condition resulting from connective tissue changes and consequent contraction. It is not due exclusively, as generally thought, to the direct influence of a transitory or long continued partial deprivation of oxygen and nourishment, nor is it due exclusively to the toxic effect of an overcharge with carbon dioxide. An important factor is the inactivity of the muscle, induced by the above mentioned directly damaging influences. The circulatory disturbances resulting from these begin and the inactivity completes the process of degenerative change. The circulatory disturbances may be due to a total interruption of the circulation for several hours by constriction of the limb or the occlusion of a large arterial trunk. In such cases a sufficient collateral circulation develops to prevent gangrene. Above all, the interstitial effusion of blood and lymph should be emphasized, since it increases the interstitial pressure. Substantial afferent and efferent branches may succumb to large interstitial effusions. Hemorrhage from very small vessels may lead to total compression of the largest arteries and veins. The efforts at expansion of small, otherwise unimportant interstitial effusions, may prove dangerous when resisted by some unyielding resistance. Thus a plaster of Paris cast may lead to most severe disturbances of the circulation, in some cases even to gangrene. The primary damaging influence of free effusions comes from the occlusion of smaller or larger arterial paths as well as from the suppression of the terminal collateral branches, not wounded but subject to venous pressure. The latter is especially worthy of attention because the retardation in the arterial capillaries interferes with the supply of oxygen and other nourishment and is combined with the direct toxic effect on the tissues which is most marked in the venous system from carbon dioxide. With inactivity the transforming strength of muscle movement is eliminated. In muscle movements are included the active and passive, and included among the latter are

massage, passive gymnastics, and electricity. They stimulate the circulation of the blood and lymph and may be a factor in the preservation of the extremity threatened by the stasis. The part played by the nerves in isehemie muscle contracture is difficult to determine.

Acute Gastric Ulcers Perforating into the Peritoneal Cavity.—WAGNER (*Deut. Zeitschr. f. Chir.*, 1913, cxx, 438) says that the only rational treatment for these cases is early operation. Operation within twelve hours gives a favorable prognosis, but after this time the prognosis becomes rapidly unfavorable. Since, however, cases with late peritonitis have been saved by operation, this becomes the last resort in late cases. As soon as a severe symptom is recognized, indicating an acute severe disease in the abdomen, as appendicitis, perforation of the intestine, gall-bladder, etc., the patient should be assigned to the surgeon. Only through early operation can the still frightful mortality be further reduced. By exact attention to the history and symptoms, among which the initial pain and muscle defense occupy first place, an exact diagnosis is possible in two-thirds of the cases. Morphine is to be avoided. Weakness is not a contraindication to immediate operation. The simplest, most quickly performed and, therefore, the most rational operation is the closure of the perforation by the Lembert suture, with or without freshening of the edges, and reinforcement by suturing over it a portion of the omentum. Gastro-enterostomy is indicated only in the presence of a pyloric obstruction or an hour-glass stomach. Excision or resection, as a rule, makes too great a demand upon the strength of the patient. If suture is impossible it may be replaced by covering the perforation by omentum or a gauze tampon. For the cleansing of the unclean peritoneal cavity, the best treatment is the sparing irrigations with warm physiological saline solution without unnecessary mechanical insult of the peritoneum. With less escape of the gastro-intestinal contents, a sponging out will be sufficient. Drainage with rubber tubes rarely does damage, but frequently prevents retention of secretions and abscess formation. In the after-treatment, the stomach should be spared by the copious administration of physiological salt solution, subcutaneously and by the rectum.

Subcutaneous Contusions of the Pancreas.—HAGEDORN (*Zentralbl. f. Chir.*, 1913, xl, 124) saw last summer, almost at the same time, 2 cases of subcutaneous contusions of the pancreas, in each of which operation was performed and the pancreas exposed. While much has been published on pancreatic diseases in recent years, little has been written of the injuries, especially of the isolated subcutaneous contusions of the pancreas. Both cases were very similar as to the kind of trauma at fault and the symptomatology, although one came to operation in the acute stage, the other later. In the first case three days before admission, the wheel of a heavy wagon passed over the upper part of the abdomen. The patient soon began to vomit and to be very ill and was taken to the hospital. The vomit was dark, the abdomen distended, tympanitic and slightly tender, pulse small and rapid, temperature normal, urine free of albumin and sugar, and there had been no passage of feces or flatus for several days. Gastric irrigations brought up considerable dark fluid contents, and some

relief followed, as indicated by no vomiting, the passage of flatus, a soft abdomen, and later passage of feces. This improvement continued for five days, when the severe symptoms set in again. Relief again followed gastric irrigations, which were repeated every few days. Then the patient gradually sank again and became of a grayish sallow color, emaciated, and apathetic. The temperature remained normal, but the pulse was 120 and small. Fourteen days after admission, a laparotomy showed an abundant bloody-serous fluid among the distended coils of intestine. The serosa was smooth and without adhesions. The omentum, mesentery, and fat appendages, were closely covered with numerous sulphur yellow, small nodules, and the mesenteric lymph nodes were swollen. The stomach and intestines showed no injuries. Two coils of small intestine were adherent to the pancreas by a brawny yellowish layer, about the size of a fifty-cent piece. Palpation could not detect any wound of the pancreas. Drainage was provided by tampon of the pancreas through the mesocolon, and the fluid was sponged from the abdomen. The wound was sutured about the drainage tampon. An abscess of the parotid developed later and was drained. Gradually recovery took place and eight weeks after the operation the patient left the hospital healed and strong. The second patient suffered the same accident as the first and showed very much the same symptoms. In the right lung there developed a dull area, laterally and below, and there was dullness in the lower abdomen. On the following day the patient showed marked collapse and was operated on immediately. The intestines were distended, the diaphragm was uninjured, but between the coils of intestine was some blood stained serous fluid. The serosa was smooth, but the omentum and mesentery were covered with typical sulphur yellow fat necroses. Exposure of the pancreas, to sight and palpation, showed that the pancreas was uninjured. The healing was without disturbance. There was no sugar in the urine, and eight days after the operation the patient was free of all disturbances. Sixteen days after the operation he was discharged.

Treatment of Total Rupture of the Urethra.—HOFMANN (*Zentralbl. f. Chir.*, 1913, xl, 155) in three cases of total, traumatic rupture of the urethra, did the following operation, after unsuccessful attempts at catheterization: After opening the bladder, a specially constructed metal catheter was passed through the internal orifice of the urethra to the site of the rupture. An incision was then made upon the beak of the instrument, exposing the latter. Now a partially flexible special catheter was mounted on the beak of the metal one and drawn out through the bladder and abdominal wall. The same metal catheter was then passed through the urethra from the meatus until it emerged at the site of the rupture, when the other end of the flexible catheter was grasped again in the same manner as before and was drawn outward through the urethra. The further care of the wound was conducted in the usual manner. The two ends of the soft catheter emerging from the bladder and urethra were tied together by a silk ligature. In this way the soft catheter could be drawn backward and forward daily, which contributes to the reestablishment of the new bridge of mucus membrane. In the three cases operated on, soon after the removal of

the catheter, spontaneous urination was possible and the ruptured area healed without stricture. The only difference between the metal catheter and the usual one is that the beak is so formed that the channel of the catheter is continued from the side opening at the end in a groove to the tip, the end being conical. The end of the partially flexible catheter is small and so shaped that it fits into the groove in the beak of the metal catheter, and upon a pull on the latter both become locked together. Two figures illustrate these important alterations in the ends of the two instruments.

Chronic (Non-suppurative) Hemorrhagic Osteomyelitis.—BARRIE (*Annals of Surgery*, 1913, lvii, 244) says that the lesions in the ends of the long bones described as medullary giant-celled sarcoma, myelogenous giant-celled sarcoma, myeloma, and giant-celled tumor, should not be included in the classification of tumors. The process begins as the result of a trauma, and gives all the clinical and pathological evidence pertaining to a low grade inflammation. The foundation upon which the diagnosis of malignant tumor has been based is the presence in the tissues examined under the microscope of numerous giant-cells which do not show any uniformity of architectural arrangement or boundary zones. It is an established fact that these giant-cells are not tissue builders, but scavengers, whose function is the removal of debris that is produced by low-grade inflammatory conditions occurring in bone. The whole process is explained on the basis of the lesion being due to a low-grade, ever present irritation or inflammation, which causes excessive production of vascular granulation tissue masses. From the clinical picture and the gross and microscopic pathology the condition presents, the term chronic (non-suppurative) hemorrhagic osteomyelitis seems a more correct definition of the lesion than the terms now in use.

Renal Tuberculosis in Children. Catheterization of the Ureters by Direct Vision.—ROCHER and FERRON (*Jour. d'Urolog*, 1913, iii, 153) report 6 cases in which catheterization by direct cystoscopy was employed with the patient under the affects of an anesthetic, local or general. The patient was placed in the Trendelenburg position and a urethroscope, No. 50, 7 cm. long, was introduced without great difficulty. The bladder was widely dilated with air. The mucosa was very red and presented ulcerations in the trigone on the left side. The orifice of the right ureter was normal while the left was replaced by a large black hole into which a No. 8 sound penetrated easily. Immediately about 10 c.c. of purulent urine escaped. The left kidney was removed. About two months later the patient had gained 3 kilograms in weight, was in good general condition, but the frequency of micturition persisted. They conclude that cystoscopy by direct vision is always possible, even easy, in a girl, aged over five years. The urethra admits easily a No. 40 tube, 7 cm. long, and notwithstanding the restricted field, the shortness of the tube permits the exploration of the bladder. In cases with a tolerant bladder, a mild Trendelenburg position suffices for the vesical distention, and this position is easily tolerated at this age. The bladder in the girl is analogous to that of the woman. While the interureteral band is often slightly marked,

it may be distinct. The ureteral orifice generally admits a No. 6 or 7 sound. In one of their patients, both ureteral meati admitted only a very fine bougie. This disposition does not depend on the age. They have encountered it in adults and all specialists have seen it. General anesthesia was frequently employed, not because the manœuvres were painful, but because very often the children were frightened by the instruments and became unmanageable.

The Abortive Treatment of Acute Gonorrhea.—LEBRETON (*Jour. d'Urolog.*, 1913, iii, 203) discusses the various substances and methods in use for the abortive treatment of gonorrhea and reviews extensively the French literature of the subject. By procedures of different kinds, limited or not to the anterior urethra, with the aid of very variable substances and doses, all the authors reviewed have obtained results that were often excellent and sometimes even remarkable. But there is no single method which is sure to give definite results. This is due to the fact that the disease does not always act in the same way, but its course varies according to factors which it is impossible to determine from the beginning. The results are sufficiently good to make it advisable to try the method whenever it can be done reasonably. It reduces the annoyances and complications which are always possible with an affection so tenacious and so dangerous as gonorrhea. The method to be selected from all those reviewed varies according to the particular case.

Clinical, Pathological, and Therapeutic Studies Concerning the Gastric Crises of Tabes Dorsalis.—CADE and LERICHE (*Deutsch. Zeitsch. f. Chir.*, 1913, cxxi, 41) discuss this subject at length, Cade from the medical side and Leriche from the surgical. In determining the method to be chosen and the procedure to be followed, when the indication for surgical interference arises in a tabetic patient, one should first attempt to recognize the nature of the crisis and to distinguish its chief elements. If the crises are very painful, with much vomiting, tachycardia, intermission of the pulse and laryngeal crises, one must fear a vagus involvement. The evidence of it should be sought and then the performance of a double-sided vagotomy, according to Exner, may be considered. This type of case, however, is the exception. Usually we have to deal with sympathetic crises. In these, we should proceed from the simplest methods of treatment to the most complicated operations. The most benign treatment should be tried first and the most severe reserved as the last resort. The simplest is that of König, who injects into the muscles of the back, on both sides of the spinous processes, 100 c.c. of a 0.5 per cent. solution of novokain. A lasting effect can probably be produced by the substitution of alcohol for the novokain and thus we treat the gastric crises as we do a facial neuralgia. If this method fails, Franke's operation may be tried. The fifth to the seventh intercostal nerves are excised (the number is determined by the result of the combined gastro-intestinal symptoms). After this, one may try the Jaboulay operation, that is, the stretching of the solar plexus. Should this method fail or be followed by recurrences, recourse may be had to the Forster operation, seven roots on both sides being divided, if possible. If the

patient is capable of the necessary resistance and the crises are very severe, with a considerable participation of the intestines, the immediate division of the spinal roots should be undertaken. It would be very surprising if one did not succeed with one of these procedures, in giving these patients relief from their severe distress.

A Contribution to the Serum Diagnosis of Malignant Tumors.—BRÜGGEMANN (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxv, 877) calls attention to the interest shown in recent years in the serum diagnosis of malignant tumors. Although a series of reactions have been suggested for the diagnosis of the tumors from the blood stream and many authors have made investigations, the results are not yet satisfactory. In his investigations, Brüggemann employed chiefly the hemolytic test of Kelling and the meiotagmin reaction of Ascoli, although in a small part of the patients the Wassermann reaction was tried. Kelling found that in 66 per cent. of the patients with malignant tumors of the digestive tract, the serum produced a considerably stronger and more rapid hemolytic effect on the red blood corpuscles of hens, than the serum of patients with other diseases or healthy patients. With his test he was able in many cases, in which no tumor could be felt, to make a correct diagnosis as was demonstrated by later operation. Kelling designated his tests as IIa, IIb, and III. The IIa test determines the amount of hemolytic ferment in the serum, which is increased in malignant tumors. The IIb test shows the existence, according to Kelling, of a specific immunizing body combined with the red blood corpuscles of the hen. The III test shows that a certain amount of the specific immunizing body becomes, through inactivation for the red blood corpuscles of the hen, incapable of combination. Brüggemann employed Kelling's tests on the sera of 159 patients and on the sera of 16 pregnant women. He found that the tests IIa and IIb were not useful for the diagnosis of malignant tumors in general. In malignant gastric tumors, in the diagnosis of which Kelling specially advised the tests, the results were strikingly more frequently positive (68 per cent. of the cases) than with other gastric diseases (only in 7 per cent., or in 3.5 per cent. if those cases which had fever a short time before were excluded). This high percentage of positive reactions in malignant gastric tumors is particularly due, in Brüggemann's opinion, to the fact that marked destruction of the cancer, as it is seen in the stomach and intestines as well as in the ulcerated cancers of the mamma and uterus, causes a marked hemolytic effect in contrast to nonulcerated malignant tumors. A markedly positive result with test IIa in the case of an abdominal tumor, taken with other symptoms, supports the diagnosis that the tumor is in the gastro-intestinal canal or has invaded the canal. The test III gave irregular results although the number of cases investigated are admitted to be small. In a part of the positive results with the tests IIa and IIb, the weak reactions were probably due to the increased quantity of the normally occurring nonspecific hemolysins, in another part of the cases to the destructive products of the malignant tumors, which cause a strong hemolysis. The pregnant women showed a striking frequency of weak positive reactions. The meiotagmin reaction of Ascoli does not give a specific reaction for malignant tumors,

although one cannot deny that it has clinical value. Cachectic conditions not due to malignant tumors always gave a negative reaction. It can be an aid in the diagnosis of malignant tumors and will probably be generally adopted when the technique is made more simple.

THERAPEUTICS

UNDER THE CHARGE OF

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A New Cathartic for Subcutaneous and Intramuscular Administration.—CREDE (*Münch. med. Woch.*, 1912, lix, 2868) writes concerning sennatin which he isolated as the active principle of senna. He reports excellent results from its use subcutaneously or intramuscularly. He tried it in 300 cases and found it produced a bowel movement in about 83 per cent. of the cases. He advises its use in peritonitis and ileus, also as a prophylactic measure against postoperative intestinal paralysis. The remedy appears to have no toxic effects and produces practically no local reaction when given intramuscularly.

The Value of Pertussis Vaccine.—SCOTT (*New York Med. Jour.*, 1913, xevii, 176) reports 17 cases of pertussis treated with vaccines. Most of the cases were cured and in all the remaining cases the symptoms were distinctly improved. The number of attacks became less, their severity was diminished, cyanosis was less marked or vomiting during the paroxysms ceased. Children slept better, mainly because the attacks at night were less marked. The author advises an initial dose of 40,000,000 bacteria and gives the following doses with reference to the effects following the last dose. If much benefit arises he prolongs the intervals between the injections; if little or no benefit, he shortens them. He says that his experience seems to indicate that larger doses of vaccine should be given in the earlier stages of the disease. He also believes that infants require relatively higher dosage but fewer injections than do older children. The injections did not produce any local reactions. Scott believes that it is better to give a dose of 40,000,000 at short intervals for the treatment of severe cases rather than larger doses not so frequently repeated.

The Emetic Action of the Digitalis Bodies.—EGGLESTON and HATCHER (*Jour. Amer. Med. Assoc.*, 1913, lx, 499) say that the opinion is well-nigh universally held by clinicians and pharmacologists that the nausea and vomiting which sometimes follow therapeutic doses of the digitalis bodies are due to their direct irritant action on the gastric mucous membrane. Analysis of the literature shows that this opinion is based on deductions, and not on experimental evidence

obtained with therapeutic doses. This is wholly apart from the recognized fact that massive doses of these bodies applied directly to the gastric mucous membrane do cause irritation. The authors' experimental work on animals showed that all of the digitalis bodies caused nausea and vomiting when moderate doses were introduced into the circulation. They explained this action by a direct effect on the vomiting centre of the medulla and it was also found that vastly larger doses of some of these drugs could be introduced into the stomach without causing nausea or vomiting, and in such cases it was subsequently shown that little absorption into the blood stream had taken place. They believe that we have no means at present of securing the cardiac actions of the digitalis bodies without subjecting the vomiting centre to the influence of these agents at the same time, and there is no advantage in substituting one mode of administration; or one member of the group, for another, and the employment of opium to prevent the gastro-intestinal symptoms of the digitalis bodies in ordinary cases masks the appearance of toxic symptom which should serve as a signal for the reduction of the dose. The authors state that their results certainly lend no support whatever to the claims made that digalen, digipuratum, digitalysatum or the fat-free tincture of digitalis are in any way less actively nauseant or emetic in proportion to their cardiac activity than any of the better known and less expensive galenical preparations of digitalis and strophanthus.

Benzol in the Treatment of Leukemia.—BILLINGS (*Jour. Amer. Med. Assoc.*, 1913, lx, 495) reports 5 cases of leukemia treated with benzol. Four of these patients suffered from myeloid leukemia and one from a rather atypical type of lymphoid leukemia. All but one of the patients had received x-ray treatment before the benzol was begun. Röntgenotherapy was used in connection with the benzol treatment with all of the patients except in one patient where a severe x-ray burn prevented its use. Billings reports the cases in detail and a brief summary of his results in the individual cases is of great interest. The first patient had shown phenomenal improvement under x-ray treatment but had relapsed, and a severe x-ray burn necessitated the withdrawal of this method of treatment. At the beginning of the benzol treatment he had approximately 200,000 leukocytes, with a rather large percentage of myelocytes. Under the use of the benzol, the leukocytes melted away and three weeks after the drug had been withdrawn the fall continued and reached the low count of 3,600, with no myelocytes. With the great drop in the whites, the red cells amounted to about 5,000,000, and the hemoglobin from 85 to 90 per cent., so that while there was a destruction and removal from the peripheral circulation of the leukocytes, both reds and hemoglobin improved. There was a corresponding improvement in the patient's general condition; a gain in weight of 5 pounds, a feeling of well-being and lessened nervousness especially of the tremor from which he had suffered during his whole illness. The second and third cases require no special mention except for the fact that both patients had x-ray treatment for months with progressive improvement in the blood picture and also that there was diminution in size of the spleen; but

this improvement was slow and finally came to a stand. Under the use of both x -rays and of benzol the improvement became much more rapid, with corresponding improvement in general health. The fourth case deserves special mention because of the remarkable effect of the treatment. The patient had had two or three x -ray treatments before the benzol was begun on November 13. The first effect which was produced within six days, was to increase the number of leukocytes from 546,000 to 780,000. Three days later the count had fallen to 600,000; December 2, to 290,000; December 17 to 16,000, and January 5, the last examination, to 8,500. In less than two months of Röntgenotherapy and benzol treatment, the blood picture had returned almost to normal, and the myelocytes, which were found in the blood in a high percentage disappeared. The spleen, which was very large in the beginning, was just palpable on the last date. There was a corresponding general improvement in the patient's condition. In the fifth case the blood picture was that of lymphoid leukemia, but the lymph nodes were not large. The spleen was very large. With x -rays and benzol treatment the leukocyte count of 45,000 dropped to 19,000 in three days, then to 5,600 in six days. The benzol was continued experimentally, and January 5, about one month after beginning the treatment, the blood count was: hemoglobin, 68 per cent.; reds, 4,120,000; leukocytes, 5,900, of which there were small lymphocytes 35 per cent., large lymphocytes 9 per cent. and polynuclears 56 per cent. During the treatment the red cells and hemoglobin remained the same as at the beginning. The spleen rapidly diminished to not more than one-fourth the original bulk, and the small lymph-nodes disappeared. There was a marked improvement in the general condition of the patient. The benzol was usually given in gelatin capsules filled at the time of administration. One patient took the drug in an emulsion, made up by the hospital druggist, of which two teaspoonfuls equalled 15 minims of benzol. The drug was given soon after meals and at bed time. The beginning was 7 minims, which was soon increased to 15 minims. All patients complained of eructation of gas tasting and smelling of benzol. Burning in the stomach was a common symptom. As a rule the appetite was not disturbed, with one exception, and in this patient the general nutrition remained good. Of the other four all gained in weight. No other medicine was given except the necessary laxative or occasionally the mixture of rhubarb and soda as a stomachic. As a rule the patients were kept at rest. The benzol used was that obtained by the hospital druggist, and no analysis was made of it for the presence of nitrobenzol or anilin. However, Billings advises the use of a purified benzol on the ground of Selling's statement that impure benzol contains nitrobenzol and other products (anilin, etc.), and that anilin is the probable toxic substance producing purpura hemorrhagica, aplastic anemia, etc.

Antityphoid Vaccination in Children.—RUSSELL (*Jour. Amer. Med. Assoc.*, 1913, lx, 344) says that the prophylactic use of antityphoid vaccine among children has, as yet, received scant attention in medical literature. He believes that this measure is highly desirable for children from two to sixteen years of age, who leave home for

summer vacations, schools, and colleges. Russell gives statistics based on the records of the inoculation of 359 children, between the ages of two and sixteen years, who have been vaccinated by fifty different physicians in many parts of the United States. The dosage is based altogether on body weight and not on age; the child is given that portion of the adult dose which his weight bears to the average adult weight, 150 pounds. If the fraction proves inconvenient a little more, rather than less, is administered. As with adults the best time for inoculation is 4 o'clock, or later, in the afternoon, since any reaction will then come after bedtime. No harmful effects have been reported in any of the 359 children and, so far as known, none has contracted typhoid fever, although some of the vaccinations were made over three years ago. Revaccination in children should be undertaken earlier and oftener than in adults, since children are immunized on a basis of body weight, and consequently should be given a second course of two or three doses when the weight shows a very material increase. In the absence of final information as to the duration of the immunity it is probably advisable to revaccinate at least every three years in every case. Further experience may show that longer intervals are permissible.

Syphilitic Aortitis: Its Diagnosis and Treatment.—LONGCOPE (*Arch. of Int. Med.*, 1913, xi, 14) reviews the literature concerning syphilitic aortitis and gives his personal observations regarding 63 cases in which syphilitic aortitis was proved to exist at autopsy or in which the diagnosis seemed reasonably sure from the combination of certain symptoms and signs with a positive Wassermann reaction during life. His conclusions are that syphilis produces a characteristic lesion of the aorta, which is responsible, as shown by autopsy statistics and the Wassermann reaction, for most aneurysms, about 75 per cent. of cases of aortic insufficiency in adults, many cases of dilatation of the aorta, and a certain group of cases of angina pectoris. The infection of the aorta probably takes place during the secondary stage and though the symptoms and signs of syphilitic aortitis with the complications may develop within a few months of infection, the process usually remains latent or unrecognized for an average of sixteen to seventeen years. Thus syphilitic aortitis is probably a common cause for the presence of a positive Wassermann reaction in so-called latent syphitis. The early symptoms and signs of syphilitic aortitis are a positive Wassermann reaction, precordial pain, slight dyspnea, attacks of paroxysmal dyspnea and angina pectoris, cardiac hypertrophy, increased pulsation of the vessels of the neck, and signs of dilatation of the aorta. Of the entire number of cases reported 20 were treated with salvarsan. Longcope says that the precordial pain, paroxysmal dyspnea, and angina pectoris are temporarily or permanently relieved by repeated injections of salvarsan, but in certain instances these symptoms, especially after large doses, may be aggravated for the first forty-eight hours after injection. The permanent relief of these symptoms can only be obtained, if at all, by the most persistent treatment. It is probably difficult to reach the spirochetes by the blood stream so that the diseased aorta is hard to attack. Longcope is impressed with the necessity of giving repeated

doses of salvarsan and with this method recurrences are not as frequent as formerly. He thinks that possibly neosalvarsan may prove more efficacious, or the combination of salvarsan with injections of mercury. The article is a valuable contribution to the subject and includes details of the cases observed by Loncope with a summary of the pathological changes of the disease.

Epidural Injections in the Treatment of Sciatica.—LANGBEIN (*Deutsch. med. Woch.*, 1913, xxxix, 20) reports 12 cases of sciatica treated in the last two years by epidural injections of novocain. Seven of these patients were permanently cured. Syphilis was a factor in one case that resisted the treatment. One patient improved temporarily but Langbein thinks that the trouble in this case was muscular rheumatism. He attributes the lack of improvement in 2 other cases to a probable exaggeration of their symptoms. Langbein gives the technique of epidural injections as practised by him in detail. One gram of novocain, $\frac{1}{4}$ of a gram of sodium bicarbonate and $\frac{1}{2}$ gram of sodium chloride are dissolved in 100 c.c. of cold distilled water. This mixture is injected into the sacral notch between the tubercles. In fifteen or twenty minutes after the injections all symptoms of the sciatica disappeared but he left the patients in bed for a few days. He advises the use of these epidural injections for cases of sciatica that fail to benefit after two weeks' treatment by the usual antirheumatic remedies.

PEDIATRICS

UNDER THE CHARGE OF

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Addison's Disease in a Boy, Aged Ten Years.—FREDERICK LANGMEAD (*Lancet*, 1913, clxxxiv, 449) reports a case of Addison's disease in a boy, aged ten years. The reported cases of this disease in children show that the general symptoms are similar to those in adults, although in children the greater number of cases run a very acute course, the pigmentation is less obvious, and death from coma and convulsions occurs more frequently. The present case lived but four hours after admission to the hospital. Pigmentation had begun about one year before, and attacks of diarrhea with increasing weakness had followed. The boy's father, two aunts and an uncle died of tuberculosis. The symptoms of the last attack were abrupt vomiting, restlessness, unconsciousness, flexed elbows, wrists and knees, subnormal temperature, and frequent convulsive seizures. The diagnoses of meningitis, uremia, and cyclic vomiting were entertained, but were ruled out by clinical findings, and no definite diagnosis was formed. Autopsy showed slight, general pigmentation with maculæ. The suprarenal glands were fibrocaseous throughout. Caseous foci were found in the portal fissure and the lowest lobes of the lungs. Microscopically,

giant-cells and tubercle-bacilli were found. The thymus, tonsils, the lymphatic particles of the tongue and intestines and mesenteric glands were hyperplastic. The heart weighed only 3 ounces, the small size being, no doubt, due to the accompanying weakness and the low blood pressure.

A New Disease-picture in Spasmophylic Diathesis.—RICHARD LEDERER (*Wien. klin. Woch.*, 1913, xxvi, 286) describes a hitherto unreported symptom-picture in children with spasmophilic diathesis. The respiration became very slow, difficult, and harsh. The dyspnea was usually expiratory and accompanied by a high grade of cyanosis. The spasmophilic attacks were usually acute, severe, and fatal, especially so in cases of laryngospasm or convulsions. Areas of impaired resonance with bronchial breathing and frequently rales were found throughout the lungs. The cases showing rales always showed a temperature of 38° to 39° C. and the condition in these cases was thought to be a pneumonia. On autopsy, however, there appeared absolutely no signs of a pneumonia. On the other hand, large areas of atelectasis were present, running deeply into the lung, and the intervening lung-tissue was emphysematous. Up to this time nothing was known of the spasmophilic action upon bronchial, smooth muscle. In these cases it was found there was a spasm of the small bronchial muscles, the lumen of the tube was shut off, and the alveoli were isolated from the external air, thereby becoming atelectatic. The rales were produced by local edema and transudation, due to circulatory stasis similar to the edema accompanying other spasmophilic manifestations.

Multiple Calcification in the Subcutaneous Tissue.—F. PARKSE WEBER (*British Jour. Child. Dis.*, 1913, x, 97) reports a case of "calcinosis" in a girl, aged seven years. There were a large number of hard nodules in the subcutaneous tissue of the extremities and adjoining parts of the trunk. The lymphatic glands of the groin, axilla, and neck were moderately enlarged. The nodules gave no pain or tenderness, except where the skin over them was adherent or ulcerated. The blood and urine were negative. The calcium index of the blood was 1.36, the normal average being 0.9. The duration of the nodules had been one year. During the preceeding year and a half the child had successively scarlet fever, diphtheria with paresis of the legs, pneumonia, abscesses of the axilla and neck, corneal ulcer, and otorrhea. The nodules were composed of calcium carbonate and calcium phosphate imbedded in a spongy framework of connective tissue. No uric acid or tubercle bacilli were found. The Wassermann and von Pirquet reactions were negative and the muscles and bones of the body were not affected. The condition seems to be similar to that found in scleroderma with subcutaneous calcification.

Antityphoid Vaccination in Children.—FREDERICK F. RUSSELL (*Jour. Amer. Med. Assoc.*, 1913, lx, 344) refers to the prophylactic use of antityphoid vaccine in children, and presents statistics based on 359 cases, aged between two and sixteen years, vaccinated by fifty different physicians in the United States. Russel believes it

highly desirable that all children aged from two to sixteen years who leave home for summer vacations, schools, and colleges be protected by this method. The local reaction to the injection is rather less than in adults. The general reaction is divided into four classes, based on the temperature: Class 1, reactions absent; Class 2, mild, with temperature 100° ; Class 3, moderate, with temperature 103° ; Class 4, severe with temperature 103° . The dosage is based on body weight, not on age. The child is given that portion of the adult dose which his weight bears to the average adult weight, 150 pounds. The best time for inoculation is four o'clock or later in the afternoon. No harmful effects have been reported in any of the 359 children, and so far as known, none has contracted typhoid fever. Revaccination should be undertaken earlier and oftener in children than in adults, and a second course of several doses be given when the weight materially increases. At present revaccination is done after three years. This vaccine promises the greatest usefulness in protecting the younger ages, the most susceptible element of the population, from infection. A large proportion of the deaths from typhoid in this class can be prevented by antityphoid vaccination.

Infantile Scurvy Resembling Acute Articular Rheumatism.—LOUIS FISCHER (*Jour. Amer. Med. Assoc.*, 1913, ix, 279) calls attention to the development of scurvy from canned foods in which the anti-scorbutic factor is wanting. No infant fed on breast milk acquires scurvy. Cow's milk must be fed in such a manner that it is not deprived of its enzymes. Boiling or prolonged steaming devitalizes milk and tends to develop scurvy. Fischer reports the case of a thirteen months' child who suddenly refused to stand. The slightest handling of the joints of the arms and legs gave severe pain and a diagnosis of articular rheumatism had been made. There was marked tenderness over the joints. The gums were soft and tender and had a bluish-red ridge around the teeth. The child weighed twelve and one-half pounds when aged thirteen months. There was a marked rachitic rosary. The infant was bottle-fed from birth, receiving condensed milk for one month and malted milk for seven months. The etiologic factor was the absence of fresh, live food, and the diagnosis of scurvy with rickets was warranted. The treatment consists in giving orange juice, pineapple juice, and expressed beef juice, raw white of eggs and very small doses of olive or cod-liver oil if the child can assimilate them.

O B S T E T R I C S

UNDER THE CHARGE OF

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The Prevention of Ophthalmia Neonatorum.—VON HERFF (*Archiv f. Gynäk.*, 1912, Band xeviii, Heft 1) draws attention to the value of sophol as a prophylactic against ophthalmia. This substance in solu-

tion contains 18.5 per cent. of silver, and in over-saturated solution, 19.7 per cent. Tablets containing 25 centigrams are added to cold water to make a 5 per cent. solution. The tablets dissolve very slowly, but nothing should be added to make them dissolve, and the solution should not be warmed. It is used in the eyes as solutions of nitrate of silver are commonly employed.

The Treatment of Eclampsia.—FREUND (*Archiv f. Gynäk.*, 1912, Band xcvii, Heft 3) states his conclusions from the treatment of 551 cases of eclampsia in Franz's clinic in Berlin. He believes that, as we do not know the cause of the disorder, we must in a great measure use palliative treatment. He is in favor of the prompt and rapid emptying of the uterus in the interests of mother and child. There is need of a study of statistics as to the conditions and results between the first convulsion and the complete termination of labor. After the uterus has been emptied the condition of the kidneys and other eliminating organs must be carefully ascertained, and treatment instituted accordingly. In postpartum eclampsia when the pulse is hard and the tension high, bleeding is of especial value.

Rupture of the Uterus through the Scar of a Previous Cesarean Section.—JOLLY (*Archiv f. Gynäk.*, 1912, Band xcvii, Heft 2) reports the case of a rachitic patient who had a Cesarean section with a uterine incision 12 cm. long in the posterior wall, with the delivery of a healthy child weighing seven pounds. The uterus was closed with catgut. During the first eight days the patient suffered from fever, which at one time reached 104°. Mother and child were discharged from the hospital on the twenty-second day after the operation. Six months later pregnancy again occurred, and it was determined to perform Cesarean section with sterilization. The patient entered the hospital and labor began with vigorous pains. The os admitted two fingers, the membranes were unbroken, and the pulsating umbilical cord could be felt through the membranes. The patient was prepared for operation. When disinfecting the abdominal wall it was observed to be uneven and considerably tense. On examination the fetal parts could be felt directly beneath the abdominal wall. Apparently the uterus had ruptured during the patient's transfer from the hospital ward to the operating room. The abdomen was immediately opened, when the child and placenta were found free in the abdominal cavity. The child was delivered viable and living, weighing seven and one-half pounds. The uterus had ruptured through the old scar. As the patient desired sterilization, supravaginal hysterectomy was performed, leaving the ovaries. Mother and child made a good recovery, and were discharged from the hospital on the twenty-eighth day. On examining the specimen it was found that half of the old scar had ruptured. The other half remained firm through its entire thickness, and could be recognized by fine white lines in the serous covering of the uterus. It was found that the posterior portion of the scar remained intact, while the anterior half upon the fundus had ruptured. On examining the specimen closely the muscle fibers had fully reformed and showed a perfectly normal structure. The serosa could be detected, and at the point where the scar had been the inferior surface of the

scar showed healthy mucous membrane. In that portion of the scar which had ruptured the appearances were different. There was an abundance of old granulation cells, connective tissue, and decidua cells had largely taken the place of muscle fibres, while the mucous membrane of the uterus had developed upon the interior surface. Between the imperfect muscle bundles there was an appearance of connective tissue. On examining the records it was found that after the first section this patient had fever on the eighth day. At that time infection must have developed through the portion of the uterine wound which afterward ruptured, and this infection prevented the formation of the normal scar. In the last thirty years in Bumm's clinic there have been 3 ruptures of the uterine scar following Cesarean section. In the first, the wound in the fundus of the uterus was closed with silk. In the pregnancy which followed the operation rupture occurred during the ninth month. Abdominal section was at once performed, and the dead child removed from the abdominal cavity. The uterine wound had ruptured throughout its entire extent. Rupture of the scar occurred in the second case, two weeks before term, the patient having already had two Cesarean sections. In the second month of the third pregnancy the patient was operated upon for ventral hernia. The scar in the uterus was then examined and was apparently normal. Spontaneous rupture occurred, however.

The Disinfection of the Hands.—SCHAEFFER (*Zeitsch. f. Geburts. u. Gynäk.*, 1912, Band lxxi, Heft 2) reviews the various methods of disinfecting the hands, and narrates his experience in the Berlin Polyclinic, which caused him to believe that it was not so much a question of the antiseptic employed as it was thorough application to the hands and of mechanical cleansing. Alcohol is considered valuable in its usual form; or acetone, whose mechanical effect is excellent.

GYNECOLOGY

UNDER THE CHARGE OF

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Vaccine Diagnosis of Gonorrhea.—The results of a series of experiments, on a rather small number of patients, with the commercial vaccine "Arthigon" are reported by NEU (*Monatsschr. f. Geb. u. Gyn.*, 1913, xxxviii, 182). This is a gonococcus vaccine, supposed to contain 20,000,000 dead organisms to each cubic centimeter. Neu says that he was induced to undertake this work on account of the exaggeratedly enthusiastic reports that have been appearing in the literature concerning the absolute specificity of various reactions elicited by gonococcus vaccines, and the resulting certainty of establishing a diagnosis in this manner. Although his series comprises but 14 cases of certain,

3 of probable gonorrhœal infection, and 9 of adnexal disease of doubtful etiology, these small numbers are more or less compensated for by the fact that all the cases were most carefully studied, being under constant observation in the ward during the entire treatment. Neu has found the local reaction—that produced at the site of injection—very uncertain and altogether unreliable; it can be slight in patients with a definite gonorrhœal infection, and strong in those who have never had gonorrhœa. The focal reaction—that occurring at the site of the disease—was practically never lacking in patients who reacted in any way at all, but in a few women with perfectly healthy genital organs a “focal reaction” occurred; that is, injection of the vaccine was followed by pain and tenderness in the adnexal regions. A general reaction—manifested by a rise of temperature of 1° C. or more—was frequently present, and was at times very marked, but even this was by no means constant. Not the slightest relation could be discovered between the intensity of this temperature rise and any therapeutic effect, as has been claimed by several authors. As a result of these investigations, Neu says that he is very pessimistic with regard to the value of gonococcus vaccine either in the diagnosis or treatment of gonorrhœa in the female, and does not believe that from the former standpoint it can be considered anything like as reliable as is Koch’s old tuberculin in the diagnosis of tuberculosis. With regard to the therapeutic effect, he has not seen in any of his cases any permanent improvement which could be ascribed to the vaccine.

Serum Treatment of Anemia Secondary to Uterine Hemorrhage.—ZUBRZYCKI and WOLFSGRUBER (*Wien. klin. Woch.*, 1913, xxvi, 95) have tried intramuscular injections of defibrinated human blood serum in 6 cases of high grade anemia consequent upon uterine hemorrhages. One of the patients was suffering from cervical carcinoma, the others from conditions diagnosticated as metropathia hemorrhagica, endometritis, etc. In all cases a marked increase in the red-cell count was observed, together with improvement in the general condition, this rise in the blood count occurring so regularly after the institution of treatment that Zubrzycki and Wolfsgruber have no doubt as to their causal relationship. (It should be noted, however, that in all cases some other method of treatment was combined with the injections—x-ray applications in 2, curettement in 2, excochleation and paquelinization in 1, hysterectomy in 1. The method employed was to obtain blood from healthy waiting women in the obstetrical wards (Wassermann in each case negative), to defibrinate this by shaking with glass beads, and then to inject from 20 to 30 c.c. of the serum into the gluteal region of the patient. From two to five injections were given, no pain or unpleasant sequelæ of any sort being seen. Nothing is said as to any permanent effect in preventing recurrence of the hemorrhage.

Dysmenorrhœa.—“Health is a perfect balance of the hormones; there are probably as many hormones as glands of internal secretion—indeed, our conception of the hormones can be expanded to consider that every organ has its specific hormone, that is, its specific metabolic product, which is poured into the general circulation.” Starting from this hypothesis, KLEIN (*Monatsschr. f. Geb. u. Gyn.*, 1913, xxxvii,

169) says that he believes many cases of dysmenorrhea are due to an insufficient loss of coagulability on the part of the menstrual blood, the result of a hyposecretion of the ovarian hormone, which he terms oöphorine, and which has been demonstrated to have an antithrombic action on the menstrual blood. On the other hand, excessive secretion of oöphorine can also cause dysmenorrhea by producing an increased swelling of the endometrium, and hence secondary colics. This type of dysmenorrhea Klein has attempted to influence therapeutically by the employment of a hormone *antagonistic* in action to oöphorine, selecting for this purpose adrenalin, since it has a vasoconstrictor action, as opposed to the vasodilator action of oöphorine. He has tried this on 35 patients in whom he considered the dysmenorrhea to be the result of endometrial congestion consequent upon hypersecretion of the ovarian hormone, with very good results in all but two. He gives exceedingly small doses of adrenalin—0.1 to 0.5 milligram—subcutaneously or by mouth. In most instances, the cramps of which the patients complained were promptly relieved, and did not recur during the remainder of the menstrual period; indeed, in a few instances, the beneficial effect appeared to continue through the next following period as well. Klein states that he considers this work purely experimental as yet, but thinks that it represents an attempt to attack the problem along biologic lines, and hence that it may lead to the discovery of a truly causal therapy.

Vulvovaginitis in Children.—RUBIN and LEOPOLD (*Amer. Jour. Dis. of Children*, 1913, v, 58) report the results of a series of investigations into the cause of the persistence of gonorrheal vulvovaginitis in young children, these investigations having been carried out upon 50 patients, all of whom were under their observation for a considerable length of time. In order to determine the relative frequency of involvement of the cervix, Rubin and Leopold have employed routinely the electrically lighted female urethroscope, using in each instance an instrument adapted to the size and age of the child. Their technique is to place the patient in the dorsal position, and then to introduce the tube, with the obturator in place, as far as it will go; the obturator is then removed, and the tube gradually withdrawn until one of the cervical lips is encountered, when the entire cervix can generally be manipulated into the end of the instrument, and studied by direct examination. If the proper sized instrument is used, this procedure should not cause trauma, pain, or hemorrhage. The value of this method of examination is shown by the fact in the majority of patients the cervix was found to bear the brunt of the infection. The vagina also was found constantly affected, the appearance varying from a general or scattered congestion to the occurrence of small hemorrhagic areas, and even small ulcerations. Occasionally small pockets, containing a drop of pus, were seen and in some instances associated with these were adhesions near the vaginal vault. The chief lesions noted in the cervix consisted of depressions or lobulations, sometimes associated with ectropion of the cervical mucosa, resembling the erosions seen in adults. Mucus or muco-pus was often seen in the crypts, between the folds, and covering a greater or lesser portion of the orifice; in some instances, muco-pus could be seen escaping from the external os after

wiping off the vaginal surface. The evidence furnished by these findings is so definite that the authors say they are able to make a positive diagnosis as to the presence or absence of gonorrheal infection in young children by means of direct inspection through the urethroscope, without resorting to smears or cultures. With regard to treatment, Rubin and Leopold are extremely pessimistic. The subjects of their investigations have been treated for three years with all the known therapeutic measures—irrigations, ointments, yeast, vaccines, sera—without any appreciable benefit. They suggest, therefore, the necessity of adopting in these cases a more active therapy, similar in a general way to that applied to the treatment of gonorrhea in adults, but consider that before beginning this the extent of the deep lesion should in every instance be accurately determined by the use of the urethroscope, the appropriate medication being carried out by means of the same instrument.

Unusual Duplication of the Genito-urinary Tract.—A most remarkable case of this condition, which in view of its extent of development must certainly be considered unique in medical literature, is reported by GEMMEL and PATERSON (*Jour. Obst. and Gyn. Brit. Emp.*, 913, xxiii, 25). The subject of the report, a healthy, married woman, aged thirty-two years, presents the following abnormalities: The anterior-superior spinous processes are 11 inches apart, and there is no symphysis pubis, a gap of $5\frac{1}{8}$ inches existing between the pubic bones. The interval between the thighs forms a perineal space 4 inches in diameter; in this are two distinct vulvar orifices, side by side, about 3 inches apart, with a single anus behind the left vulva. The vulvæ are about normal in size and form, each with well developed labia majora and minora, a clitoris, urethral, and vaginal openings. The median labia majora on each side, however, are somewhat less prominent than the lateral. Each vagina easily admits two fingers; bimanual examination reveals the presence on each side of a well formed cervix and uterus, each of which can be freely moved independently of the other. A single ovary can be felt at the outer side of each uterus. The urethræ appear normal; by catheterization 6 ounces of clear urine were obtained from the left urethra, 4 ounces of turbid urine, containing pus, from the right. By means of collargol injections through the urethræ, two distinct and separate bladders were demonstrated by the x-rays. Between and somewhat anterior to the two vulvæ is an area of skin, devoid of both hair and sweat glands. On palpation this area is found to correspond to a circular opening about $1\frac{1}{2}$ inches in diameter in the abdominal fasciæ; through this the abdominal viscera can be felt immediately beneath the thin skin. Gemmel and Paterson consider that this area represents the umbilicus, nothing else suggestive of that structure being present. One of the most interesting features about the case is that in 1910 pregnancy occurred in the right uterus, and the patient gave birth to a living male child through the right vagina; in 1912 pregnancy occurred in the left uterus, a living female child being delivered through the birth canal of that side. Both children were somewhat under-sized, but appeared to be about full term. Gemmel and Paterson ascribe all the anomalies to one underlying cause—the absence of an allantois,

and discuss the embryological features of the case at some length. Evidently there has been no median ventral diverticulum from the internal cloaca; the Müllerian ducts have remained separate, and have been drawn backward to the surface of the body, so that they have come to open separately on the surface of the cloaca before the time of differentiation of the external organs. Each Müllerian duct has then become separately differentiated into a vagina, uterus, and Fallopian tube. As a result of the lack of allantois, the pelvic girdle, although fully formed, has been arrested in development, and no symphysis pubis or mons veneris has been developed. No normal bladder has been produced, and the traction of the amnion, which must have enfolded the embryo and come in direct contact with the chorion and placenta, had favored separate connection of the Müllerian ducts with the external cloaca and the formation of bilateral bladders and urethrae out of the ventral portion of the internal cloaca. The umbilical orifice has remained patent, and a pseudumbilicus has been formed by ligation of the body wall at the time of birth.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Fundus Changes in Leukemia.—HUDSON (*Royal London Ophthalm. Hosp. Report*, September, 1911, p. 153) thus summarizes the present state of knowledge with regard to leukemia: Changes are met with in both lymphatic and myelogenous leukemia, and in both chronic and acute cases; they are, however, by no means constant, being found, according to Leber, in only one-third or one-quarter of all cases. Both eyes are almost always affected but not always in equal degree. The changes are in some cases limited to the appearance of scattered hemorrhages, while pre-retinal hemorrhage may also occur (Stoek); in other cases, however, more characteristic features are present, consisting in a light yellowish hue of the whole eye ground; distension and tortuosity of the retinal vessels, affecting more especially the veins, which are of rose tint, while the blood stream in the arteries is abnormally pale; pallor and indistinctness of the optic disk, with a diffuse haze, involving the whole retina, and often more pronounced in the course of the main veins. The veins may be bordered by white bands, while hemorrhages are found scattered through the retina, together with white spots which, according to many authors, are more numerous in the periphery of the fundus, so that they may be invisible to ophthalmoscopic examination. Such spots are also met with in the macula; they are not infrequently surrounded by a red border, and

may exhibit a definite prominence. Movement of the blood stream in the veins has been observed ophthalmoscopically. It would seem that in the acute cases fundus changes of hemorrhagic and edematous origin tend to dominate the picture, while the more characteristic fundus changes have, for the most part, been observed in chronic cases.

Paralysis of the Accommodation after Diphtheria.—OLOFF (*Klin. Monatsbl. f. Augenheilk.*, May, 1912, p. 551) observed paralysis of the accommodation, complete in the left eye and nearly so in the right, four years after a mild attack of diphtheria in a healthy young subject. No paralyses of other parts had been present. The pupillary action was preserved. Post-diphtheritic paralysis of the accommodation of six months duration and longer is extremely rare, perhaps not half a dozen cases are on record. Most authorities consider hypermetropia as a predisposing cause, in that it contributes to the strain of the weakened ciliary muscle during convalescence, which period is frequently spent in reading or other close work. Hypermetropia was not present in Oloff's case; in fact, one eye was emmetropic, and the other presented a low degree of simple myopic astigmatism. Opinions differ greatly as to the site of the lesion in this form of paralysis of the accommodation. Bumke, based upon the researches of Saenger and Wilbrand and of Nonne, thinks that the oculomotor nerve is at fault. Roemer and Stein locate the disturbance, as is the case in botulismus poison, in the small-celled median nucleus, the supposed centre of accommodation. They base their views upon the conclusions of Ehrlich regarding the poison of diphtheria. According to the latter authority, the bacillus elaborates two different substances; the one, the true toxin, causes the symptoms of diphtheria proper in the fauces, while with the other, the toxon, he succeeded in producing paralyses experimentally. The action of the latter is much slower than that of the former. Roemer thinks that this view is supported by the relative inefficiency of the serum against paralyses, the effect of which is directed against the toxin rather than the toxon. This accounts for the fact that paralysis of the accommodation is observed as frequently at present as before the administration of the serum.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Nematodes as a Factor in the Production of Cancer.—FIBIGER, of Copenhagen (*Berl. klin. Woch.*, February 17, 1913), shows some very interesting discoveries in the part played by nematodes in the causa-

tion of cancer in rats. First, his curiosity was aroused by finding three rats in the same cage affected by malignant growth of the stomach; this tumor, however, could not be grafted upon other rats. In the preparations, Fibiger saw oval holes and masses which suggested parasite bodies containing eggs. By serial sections, he found these actually were parasites, evidently a nematode; and casting about for the intermediate host, he performed 1144 autopsies on rats without definite results; he found, however, that one form of cockroach, *Periplaneta orientalis*, is the intermediate host of a filaria which is found in the rat's stomach; rats, however, fed on *P. orientalis* gave no results. Having traced his original three rats to Dorpat in Russia, he found that a sugar-refinery there was infected with *P. americana*, another variety of cockroach. Rats from the sugar refinery showed the changes so faithfully sought. Of 61 rats, 21 were negative, but 40 showed nematodes, while 18 of the 40 were affected by tumor growth, in 9 of which advanced growth like that in the original three rats was found. By feeding *P. americana* to laboratory rats, 36 out of 57 positive results were obtained. *P. orientalis* was now infected by the nematodes from *P. americana*, and now the rats fed on the former showed the same positive results. Control rats fed on control non-infected cockroaches remained free from growths. The nematode is of the genus *spiroptera*, and has apparently not been previously described. Professor Fibiger's work is a wonderful example of close reasoning and painstaking work, and it has resulted in the production of experimental newgrowths, the first method which had definitely succeeded if one except their production, unintentionally by the x-rays.

Distemper in Dogs.—The causative organism of this disease may now be considered to be definitely known: It is the bacillus bronchi-septicus of Ferry, an organism discovered at about the same time by Ferry, by McGowan, and by Torrey and Rahe, independently of one another. Extensive experiments by the last two workers, TORREY and RAHE (*Jour. Med. Research*, January, 1913) have given a large mass of accurate information. The organism is a small, slender, often paired bacillus, actively motile. In 90 cases, of the disease, they succeeded in finding bacillus in 75 per cent. It is found in the following organs, stated in the order of greatest frequency: Trachea, bronchi, lungs, nose, liver, brain, spleen, kidney, and blood. Secondary infections by other bacteria occur with great frequency. All the individual forms isolated fall within one species, as determined by agglutination tests, but one strain reduces nitrates, the other does not. The bacillus forms an endotoxin, but no exotoxins: nevertheless sterile filtrates of liquid cultures contain a free toxin, and attempts to prepare an antiserum were made by injecting toxin filtrate and bacteria, although the serum obtained a high agglutinative power it exerted no protective action. While McGowan failed to find a constant agglutinative power, Torrey and Rahe here quoted agree with Ferry in the contrary contention. The incubation period varies between four and fifteen days. The dried bacillus may remain viable for several months, but the infectivity of dried bacilli decreases rapidly, and in twenty days is lost. Susceptible dogs, actively immunized by subcutaneous injections of small doses of the bacillus, are immune to natural distemper.

Destruction of Leukocytes in the Blood Count by Thoma's Method.—MANUCHIN (*Russki Wratsch*, 1912, No. 5, S. 151) is responsible for the statement that as a result of the use of 0.3 per cent. acetic acid solution as used in Thoma's method 10 to 20 per cent. of the leukocytes present are destroyed.

Pseudotuberculosis in Man.—SAISAWA, of Tokio (*Zeitsch. f. Hyg. und Infektionskrankheiten*, 1913, lxxiii, Heft 3), describes a well observed case of pseudotuberculosis which happened in a soldier, was carefully noted throughout its course, and yielded complete bacteriological material. Before giving any particulars of Saisawa's case, it may be said that bacillary pseudotuberculosis is an infrequent disease, and few of the hitherto described cases have been given with sufficient fullness. Pseudotuberculosis is a disease most frequently of rodents, but it has been observed in mankind under the name of Zoögleic tuberculosis, and is not a clinical entity. It is caused by non-bacterial parasites such as blastomyces, actinomyces, the aspergillus group, certain protozoa, and even more highly developed organisms. Saisawa's case was caused by bacilli which were not acid fast, and correspond to the so-called "Pfeiffer pseudotuberculosis bacillus of rodents." The illness consisted of a fever with marked prostration, ending in death after ten days. There were icterus, enlargement of the liver and spleen, albumin and bile pigments in the urine, a moderate leukocytosis, in fine, a course not unlike that of typhoid fever. Blood cultures the day before death gave growths of the organism referred to above. At autopsy the most marked changes were observed in the intestines where the mucosa was swollen, slimy, and showed marked catarrhal places; there were hemorrhagic spots, Peyer's patches and the solitary follicles were greatly enlarged, and in one place there was an ulceration on the surface which lacked the appearances so characteristic of advanced tuberculous ulceration. The anatomical diagnosis gave follicular enteritis, tubercle formation in the liver and the spleen, edema of the lungs, nephritis, serous exudate in the peritoneum, pleuræ, and pericardium. The tubercles described in the liver and the spleen answer the description of the ordinary tubercle, each having a necrotic altered centre at the periphery of which small clumps of bacilli could sometimes be seen, but the bacillus tuberculosis could not be demonstrated in it. Briefly the bacilli obtained from the autopsy were the same as those obtained by blood cultures during life, and conformed to the organism above mentioned, which bears Pfeiffer's name. Saisawa carried out a very full set of observations upon various rodents, as well as upon the morphology of the organism. There has been much discussion as to the mode of infection in such cases, and Saisawa's offers arguments in favor of infection through the alimentary canal. Following this paper, Saisawa has carried out a series of experiments upon the bacillus pseudotuberculosis, he having obtained bacilli from four different sources in Europe. The five forms showed no important differences in morphology or cultivation; all are intensely pathogenic for rodents, causing a disease of an acute course with marked swelling and hyperemia of spleen, liver, and mesenteric glands, and the formation of tubercles in most of the organs. The serum reaction, agglutination, precipitation, and complement

fixation, gave unreliable results, so that these reactions offered little assistance in the identification of the different strains. One of the five stains, however, did give undoubted immunity against subsequent infections by the same, and the other forms. These bacilli are pleomorphic, usually bacillary, but sometimes coccal in form, often in diploform as well as in chains; they are non-motile, negative to Gram, stained with Loeffler's blue or carbol fuchsin show polar staining, and they grow at both room and body temperature.

The Ophthalmic Test in Glanders.—K. F. MEYER (*Jour. Infectious Diseases*, March, 1913) publishes his results in the employment of mallein dropped on the conjunctiva, as a test for the presence of glanders; this paper contains the facts regarding about 600 horses. A tested mallein preparation (in this case a 5 per cent. solution freshly made, of *mallein siccum* of Foth) is used, and 2 or 3 drops dropped on the conjunctiva of the horse to be tested. In ten and twenty-four hours, examination of the eye shows either no reaction at all, or a slimy discharge which is not counted a positive reaction, or a purulent discharge which is the requisite without which no reaction may be stated to have occurred. Should a reaction fail it is a great advantage that one may test in the same way after twenty or twenty-four hours more have elapsed. The plan offers a very useful weapon to the practising veterinarian for the detection of glanders, but is not intended to take the place of the complement fixation and agglutination tests, although present indications make it appear that it is more accurate than either one. When the serum tests are to be used, it is to be remembered that subcutaneous mallein test should be made previously.

What is the Least Lung Capacity Compatible with Life?—BERNARD, LEPLAY, and MANTOUX (*Jour. de Phys. et de Path. Gén.*, January 15, 1913, Vol. xv, No. 1) have sought to establish for the lungs the minimal capacity which is capable of sustaining life. Courmount has found that ablation of three-quarter of the lung tissue left enough to support life, but the present writers have utilized the method of producing artificial pneumothorax by nitrogen. After complete anesthesia of a dog the collapse was produced as in the human subject, with control of the amount of gas used and observation of the state of the lung by radioscopy. Briefly, they found that the lung capacity could be reduced to one-sixth and life still be supported without knowing that this is exactly true for mankind. It nevertheless encourages us to suppose that a total collapse of one lung may be produced even if the other lung be partly affected by previous disease.

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ORIGINAL ARTICLES

CLINICAL OBSERVATIONS CONCERNING TWENTY-SEVEN
CASES OF SPLENECTOMY.¹

By H. Z. GIFFIN, M.D.,

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THE association of enlarged spleen with anemia occurs in so many diseases and in such a variety of abdominal conditions that a fuller knowledge will be necessary before one can arrive at a correct classification of splenomegaly. The results of medical, surgical, pathological, and experimental experience must be reported abundantly before a correct grouping can be even attempted.

That a certain picture conforming to splenic anemia as it is clinically described presents itself there is, of course, no doubt. However, the many factors that are discussed by writers on the etiology of this condition at once make one question the advisability of stamping a given case with a certain stencil. Syphilis, malaria, passive congestion as a result of portal obstruction, thrombosis of the splenic or portal veins, the occurrence of Leischmann-Donovan bodies, the action of extraneous toxins, the occurrence of hemolysis, the existence of an undemonstrated infectious agent—these have all been considered as factors in the causation of certain cases. And there must be added to this list, after a consideration of the cases herewith reviewed, what appears to be more than an accidental association of disease of the gall-bladder, with cases that can properly be diagnosticated clinically as splenic anemia. Moreover, at one extreme, there are many histories of short duration or those without the typical symptomatology and cases with atypical blood count, while at the other extreme there are instances in which cirrhosis of the liver seems to form a slightly

¹ Read before the Mississippi Valley Medical Association, Chicago, October 22 to 24, 1912.
VOL. 145, NO. 6.—JUNE, 1913.

more prominent part of the picture than the changes in the spleen. And apart from the clinical and etiological aspects there is confusion on the pathological side. The examination of spleens removed from patients regarded from the clinical standpoint as cases of typical splenic anemia reveals no constant histologic picture. Connective-tissue increase is the common finding, but endothelial or lymphocytic hyperplasia may predominate to such a degree that the picture may even simulate a true tumor.

Where then shall the line be drawn in determining the degree of variation permissible in the cases we are to regard as splenic anemia? However, without entering further into the general discussion of conditions simulating splenic anemia, it is my purpose to present the clinical findings in those cases in which splenectomy has been done in the Mayo clinic.

The total number of splenectomies from April 6, 1904, to July 5, 1912, is 27. For convenience these are divided into three groups: (1) Those which conform closely to the clinical syndrome of splenic anemia, 18 in number; (2) cases presenting clinical features which suggest that the splenomegaly was a part of a more or less widespread infection and secondary rather than primary; (3) miscellaneous cases.

GROUP I. Splenic anemia (18 cases). Splenic anemia is at present a clinical entity. Therefore in selecting cases for this group the preoperative clinical picture was relied upon. A great and apparently uncomplicated increase in the size of the spleen and an anemia of the secondary type, usually with leukopenia, have been considered essential in the diagnosis. Where the clinical picture was complicated by any condition which would lead one to consider the splenomegaly as a secondary rather than a primary process, and likewise when the surgical pathology was definitely that of some other condition, the case was excluded. Two cases in which the spleen showed a predominating lymphocytic hyperplasia and three presenting an endothelial hyperplasia are grouped as splenic anemia because of their clinical course, and also for the reason that pathologists have not definitely decided that these conditions represent any thing more than different types of reaction.

Twelve of the patients were females and 6 males. The youngest patient was aged twenty-two years, and the oldest fifty-six years. The average age was thirty-seven years. The distribution as to decades was as follows: Between twenty and thirty years, 6; between thirty and forty years, 4; between forty and fifty years, 5; between fifty and sixty years, 3.

Enlargement of the spleen was noted in one case twenty years before operation; in another case fifteen years; in a third ten years. In 8 instances splenic enlargement had been noted less than a year preceding operation, and in the remaining 7 from one to seven years. It is probable, however, that splenomegaly had in reality been present for a longer time in many of these cases. In

14 of the 18 cases the enlargement of the spleen had definitely preceded the appearance of anemia. In no case did the occurrence of anemia clearly precede splenomegaly.

The recorded measurements of all the spleens of this group show them to be either large or enormous in size. The average length of the spleens in the 18 cases was 24 cm. All of them save 1, which lay transversely, reached below the level of the navel, and 7 extended into the left iliac fossa and beyond the median line. The largest spleen weighed 5280 grams, the smallest 425 grams. The weight was recorded in each instance; the average weight was 1680 grams. In none of them did the long axis extend diagonally across the abdomen, but lay almost entirely to the left of the median line. It is interesting to note that one spleen lay very high and the enlargement extended transversely into the epigastrium, only one-eighth of the spleen being palpable below the costal margin.

In 4 instances the contour of the spleen was not outlined definitely enough to warrant a diagnosis without the aid of a cystoscopic examination, and in 1 of these a colloidal silver radiograph was necessary to demonstrate a normal kidney pelvis. Indeed, it may be impossible to diagnosticate an abdominal tumor positively as a spleen without these procedures.

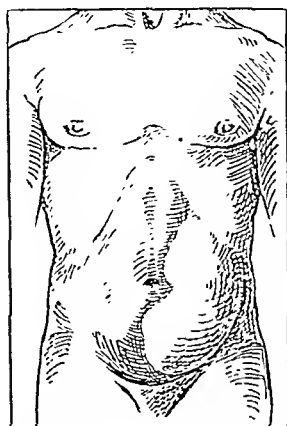
There was nothing typical about the blood in these cases save that the anemia was of the secondary type, and there was an absence of leukocytosis. The count made within a few days of operation in each case showed a hemoglobin percentage below 75 per cent. in all instances save 3; in these there had been a preceding anemia. In most of the cases an attempt had been previously made to improve the condition of the blood before operation was undertaken. In 1 the hemoglobin had been as low as 20 per cent., in another, 35 per cent. In 10 the hemoglobin had been below 50 per cent.

In 12 instances the leukocyte count was below 5500; in 1, as low as 1000. In only 1 case was a high count obtained (11,000), and this patient had been under the observation of William Osler, who regarded the condition as splenic anemia. The average of the remaining 17 cases was 4200. The occurrence of leukocytosis after operation as noted by other observers is corroborated in this series. Pain in the long bones was complained of by several patients after operation.

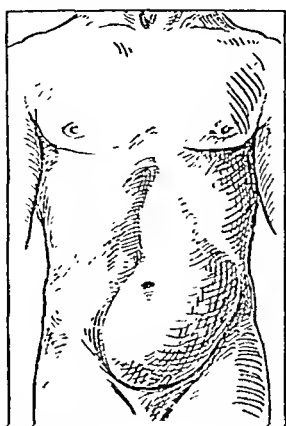
Differential counts were not distinctly abnormal, save that an occasional normoblast and megaloblast were found. The reader is referred to the accompanying blood chart for a more detailed conception of the findings.

Hematemesis occurred in 5 of the 18 cases; in 4 of these it was severe. In 1 case it had occurred every year for fifteen years. Blood in the bowel movement was also present at these times. In 1 case of Banti's disease, in which hematemesis had been severe

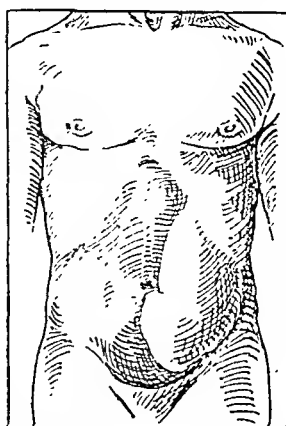
for nine months, the hemoglobin dropped as low as 20 per cent. This patient has been well for three and a half years following the operation. Another patient had had four attacks of bleeding



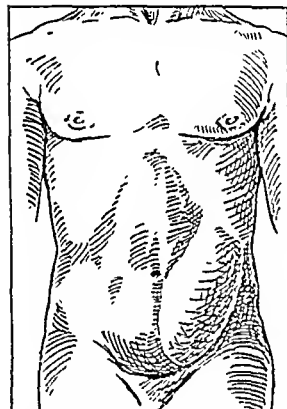
Case 1. P 3539
Splenic Anemia.



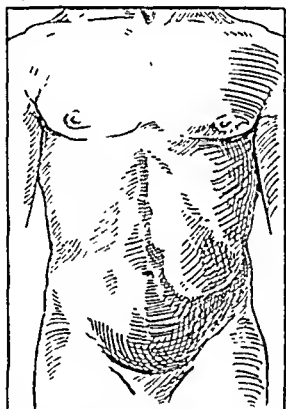
Case 2. G 8869.
Splenic Anemia.



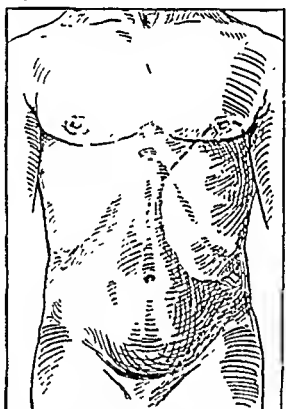
Case 3. P 7074.
Splenic Anemia.



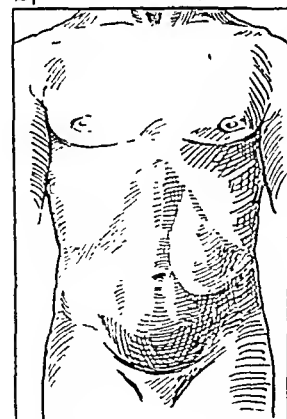
Case 4. A 9315.
Splenic Anemia.



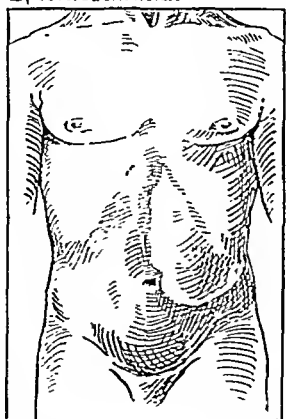
Case 5. A 10324.
Splenic Anemia.



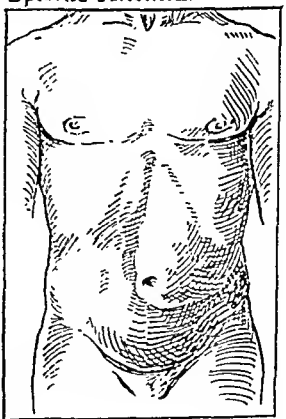
Case 6. A 18026.
Splenic Anemia.



Case 7. A 20818.
Splenic Anemia.



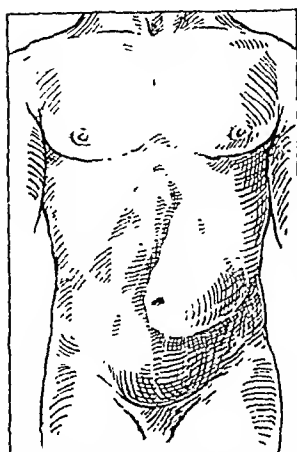
Case 8. A 22026.
Splenic Anemia.



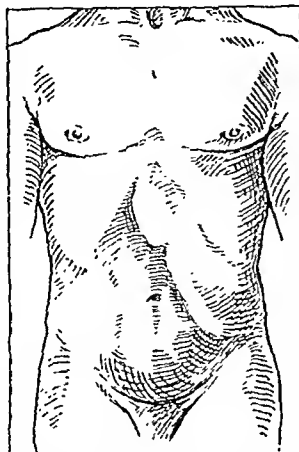
Case 9. A 27414.
Splenic Anemia.

FIG. 1.—Contour and position of spleen as observed clinically before operation.

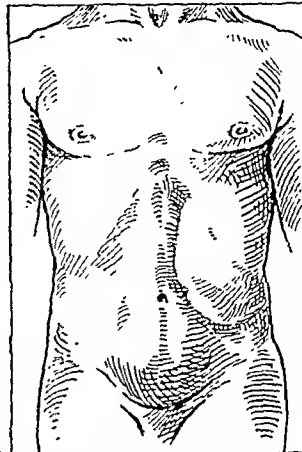
in two years; all were severe. The fourth patient had had two attacks of hematemesis, one of which occurred before splenic enlargement was noted. In the fifth patient the bleeding was



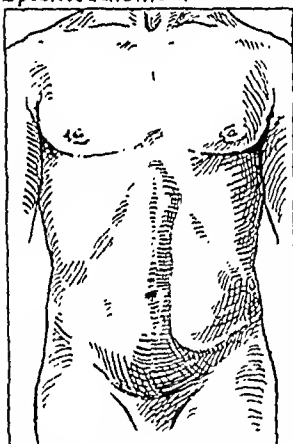
Case 10. A35431.
Splenic Anemia.



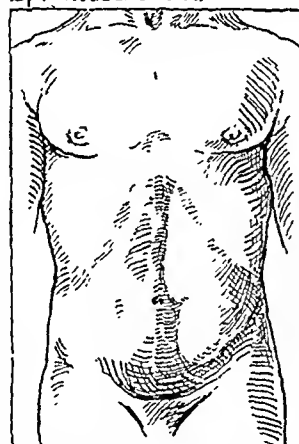
Case 11. A39665.
Splenic Anemia.



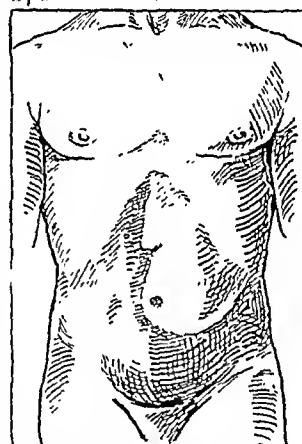
Case 12. A49050.
Splenic Anemia.



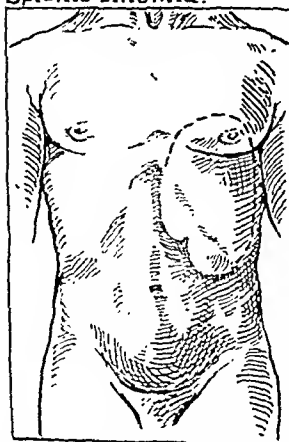
Case 13. A28194.
Splenic Anemia.



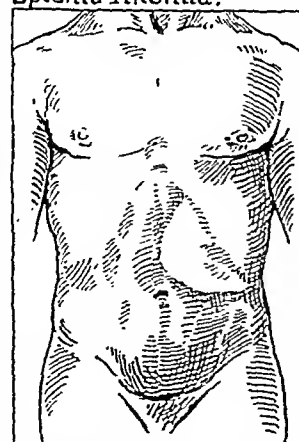
Case 14. A58017.
Splenic Anemia.



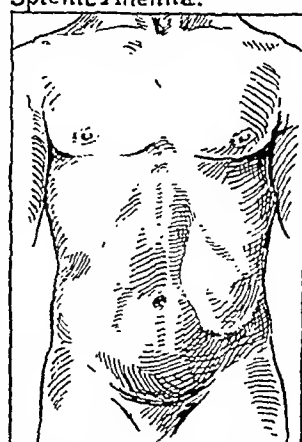
Case 15. A58751.
Splenic Anemia.



Case 16. A68578.
Splenic Anemia.



Case 17. A68788.
Splenic Anemia.



Case 18. A69913.
Splenic Anemia.

FIG. 2.—Contour and position of spleen as observed clinically before operation.

merely a regurgitation of blood. There was no instance of bleeding elsewhere than from the gastro-intestinal tract. One additional patient had spat blood probably from the throat at the time of menstruation for three years preceding operation. This has occurred much less frequently since operation.

The frequent occurrence of pain in the region of the spleen is a noteworthy incident in this series of cases. This symptom has not been generally discussed in connection with splenic anemia, and is probably caused by the perisplenitis which is so commonly present. Infarction may also be a cause of pain. In 12 of the 18 cases there was obtained a history of pain generally coming in prolonged periods at the left costal arch and often associated with tenderness. In 6 instances a history of acute attacks of pain was also obtained.

Fever was present in only two of these cases while under observation, and was not over 100°. However, cases regarded clinically as splenic anemia with fever have been reported. Two patients presenting conditions simulating splenic anemia who suffered from high fever, chills, and prostration in periodic attacks have been under our observation. These cases at first seemed to be atypical acute cases of splenic anemia. One of them at exploratory operation showed an advanced cirrhosis of the liver, and an omentopexy was done. The other is included in the second group of this series. Splenectomy was performed, but at operation evidences of gall-bladder disease were found, with many upper abdominal adhesions, and the spleen was not of enormous size. In this patient there were periodic and abrupt elevations of temperature to 105°, and at the same time the size of the spleen increased and upper abdominal pain of moderate severity was complained of. The condition of the spleen seemed to be secondary to a widespread abdominal infection, and not primary.

Diarrhea had been present in only 4 of the 18 cases. One of these was amebic and occurred in association with malaria ten years preceding operation. In another instance diarrhea had occurred in spells for one year, during which time splenic enlargement had been noted; the stool examination was negative. In the third case diarrhea had been troublesome for nine months, which was about five months preceding splenic enlargement. The fourth patient gave a history of diarrhea, which was mild and probably entirely incidental.

A history of malaria was obtained in only 4 cases. In 2 of these there may have existed some direct etiologic relationship. One patient had had malaria nearly every year up to the age of twenty-nine years, while splenic enlargement had been noted at times after the age of twenty-three years, which was twenty years before operation. Another patient, presenting a typical picture of the ascitic stage of Banti's disease, had had malaria eleven years preceding operation, at which time splenic enlargement had first been

noted. It is probable that chronic malaria produces a condition which eventually cannot be differentiated clinically from splenic anemia. The table of residences is as follows:

Alabama	1
Arkansas	1
Iowa	4
Michigan	1
Minnesota	3
Montana	1
New Mexico	1
New York	1
North Dakota	2
South Dakota	1
Virginia	1
Washington	1

A history of lues was not obtained in any of the cases grouped as splenic anemia. The Wassermann reaction was done on several of the more recent cases and was negative.

Cirrhosis of the liver was diagnosticated at operation in 5 of the 18 cases. In one additional patient clinical evidence of cirrhosis of the liver developed one year after operation, and the patient died later. In 2 other patients the liver was enlarged. In all, then, 8 of the 18 cases showed some change in the liver, while 5 were probably of the Banti type at the time of operation; 2 in the preascitic stage and 3 in the ascitic stage of Banti's disease. No case showed abdominal fluid without evidence of change in the liver at operation.

Jaundice was noted during the course of the disease twice, once with and once without evidences of cirrhosis. Melanoderma was noted in those cases seen by the writer, but no accurate information as to its occurrence in the series can be given.

The etiologic relationship of gall-bladder disease in connection with splenic enlargement may be of greater importance than is at present believed, both by reason of the possibility of infection and also through some influence upon the circulation in the closely related organs of the upper abdomen. Two cases of this series showed evidence of gall-bladder disease at operation, but the splenic enlargement was so great and the picture of splenic anemia so prominent that these cases have been retained in Group I. Moreover, 3 cases herewith reported in Group II showed gall-bladder disease, giving a total of 5 instances of gall-bladder disease in a group of 27 cases of splenomegaly (18.5 per cent.). This seems to be more than an accidental coincidence. One patient whose case was interesting in this connection had been operated on when fourteen years of age for gallstones. The gall-bladder was then removed; there were stones in the ducts and an enlarged spleen was found. Seven years later when splenectomy was done a diagnosis of Banti's disease was confirmed at operation. During the interim there had developed a progressive enlargement of the spleen with recurring attacks of anemia.

During the last two years while operating for other abdominal conditions a moderate enlargement of the spleen (three and four times normal) has been noted in 16 cases. In 8 instances it was associated with gall-bladder disease.

The operative mortality in the entire group of 27 cases was 2, or 7.4 per cent. One of these patients was in very poor condition and death occurred on the day of operation; moreover, this was an early case, the third of the series. In the 18 cases grouped as splenic anemia the postoperative results have been very satisfactory. Of the 16 patients who recovered from operation, 12 are in excellent health for periods varying from six months to seven years, 2 are improved, 1 improved for several months, but later developed ascites and died three years after operation, with symptoms of hepatic cirrhosis, and 1 died two and a half years after operation—the cause of death unknown. Of the 2 patients reported as improved, 1 shows normal blood, but is suffering from myocardial and renal insufficiency, while the other was operated upon six months ago; 4 of the 5 patients who showed evidence of cirrhosis of the liver at operation are in excellent health, 1 as long as seven years after operation. The results are shown in more detail by the following table:

GROUP I.—Postoperative Results. Cases Conforming Clinically to the Syndrome of Splenic Anemia.

Case.	No.	Year.	Time after operation.	Result.
1	(P3539)	1905	7 years	Well. Ascitic stage of Banti's disease. Spleen showed lymphocytic hyperplasia.
2	(G8869)	1907	1 day	Operative death. Ascitic stage of Banti's disease. Spleen showed endothelial hyperplasia.
3	(P7074)	1907	5½ years	Well. "Better health than ever." Spleen showed lymphocytic hyperplasia.
4	(A9315)	1908	4½ years	Well. Spleen showed endothelial hyperplasia.
5	(A10324)	1908	3 years	Improvement for several months. Death three years after operation. Ascites and dropsy (hepatic cirrhosis?).
6	(A18026)	1908	4 years	Well.
7	(A20818)	1909	3½ years	General health excellent. Ascitic stage of Banti's disease.
8	(A22026)	1909	2½ years	Death, cause unknown.
9	(A27414)	1909	3½ years	Blood normal. Myocardial and renal insufficiency. No improvement in general health.
10	(A35431)	1910	5 days	Operative death.
11	(A39665)	1910	2½ years	Well. Symptoms probably due to arthritis deformans.
12	(A49050)	1911	1½ years	Well. No hemorrhages.
13	(A28194)	1911	1½ years	Excellent health. Preascitic stage of Banti's disease.
14	(A58017)	1911	1 year	Excellent health.
15	(A58751)	1911	1 year	Well. Spleen showed endothelial remains.
16	(A68578)	1912	6 months	Improved.
17	(A68788)	1912	6 months	Gained twenty-five pounds. Better health than for years. Preascitic stage of Banti's disease.
18	(A69913)	1912	4 months	Excellent health.

CONDENSED TABULATION—EIGHTEEN CASES OF SPLENECTOMY FOR SPLENIC ANEMIA.

Case No.	Office Name.	Date of Operation.	Age	Pathology. ²	Postoperative condition.	Size of spleen.	Weight of spleen.	Duration of spleno-megaly.	Pain in splenic region.	Size of liver.	Abdominal Build.	Jaundice.	Hematemesis.	History of anemia.	History of malaria.	History of liver.	Old gall bladder disease.
1	P. G. M.	Nov. 4, '05	F. 41	Lymphocytic hyperplasia	Sept. 24, '12. Well	To pelvis	3275G	4 yrs.	Neg.	+	+1	Neg.	Neg.	6 mo.	From 8 to 14 yrs. of age	Neg.	Neg.
2	G. S. 869	Jan. 7, '07	F. 27	Endothelial hyperplasia	Jan. 7, '07. Death day of operation	30x20x8 cm.	5280G	15 yrs.	2 yrs.	+	+3	+1	Neg.	10 yrs.	Neg.	Neg.	Neg.?
3	P. 7074	May 17, '07	F. 27	Lymphocytic hyperplasia	Sept. 27, '12. Well	To pelvis	2190G	1 yr. + 1 yr.	1 yr.	Normal	Neg.	Neg.	Neg.	1 yr.	Neg.	Neg.	Neg.?
4	A. 9315	May 11, '08	F. 37	Some areas of endothelial hyperplasia	Sept. 25, '12. Well	30x20x7½ cm.	895G	9 mo. + 9 mo.		Normal	Neg.	Neg.	Neg.	?	Neg.	Neg.	Neg.?
5	A. 10324	A. V. L. July 2, '08	F. 49	Chronic splenitis	Improved for several months. Death, May 19, '11	For sev- 21 cm.	1450G	9 mo. + Neg.		Normal	Neg.	Neg.	Neg.	9 mo.	Neg.	Neg.	Neg.?
6	A. 18026	H. N. Dec. 31, '08	M. 26	Chronic splenitis	July 10, '12. Well	18 cm.	425G	2 yrs. + 2 yrs.		Normal	Neg.	Neg.	Neg.	5 mos.	Neg.	Neg.	Neg.?
7	A. 20818	C. K. Mar. 4, '09	M. 30	Chronic splenitis	Sept. 25, '12. Well	20 cm.	1180G	10 yrs.	4 yrs.	Reduced (cirrhosis)	Neg.?	Neg.	4 times severe	2 yrs.	11 yrs. before	Neg.	Neg.
8	A. 22026	J. D. B. Apr. 14, '09	F. 53	Chronic splenitis	Dec. 15, '11. Death. Cause unknown	20 cm.	1670G	3½ mo. (8 yrs.?)	8 yrs.	Normal	Neg.	Neg.	Regurgitation	4 mos.	Neg.	Neg.	Neg.
9	A. 27414	C. M. H. Aug. 11, '09	M. 45	Chronic splenitis	Sept. '12. Hb. 90. 32x25 cm. per cent. Cardiac and renal symptoms		1514G	4 yrs.	4 yrs.	Normal	Neg.	Neg.	Neg.	2 mos.	Neg.	Neg.	Neg.
10	A. 35131	W. J. P. May 3, '10	M. 39	Chronic splenitis	May 9, '10. Death on fifth day	25x20 cm.	575G	15 yrs.?	2 mos.	Normal	Neg.	Neg.	Once a yr for 15 yrs.	15 yrs.	Neg.	Neg.	+
11	A. 30665	T. O. B. July 4, '10	F. 50	Chronic splenitis	Oct. 19, '12. Well. 30 cm. Arthritis deformans		1385G	4 mo. + 3 mos. (9 mo.?)		Normal	Neg.	Neg.	Neg.	6 mos.	Neg.	Neg.	Neg.
12	A. 49050	F. F. Feb. 27, '11	M. 23	Chronic splenitis	Aug. 22, '11. Well	24x20 cm.	879G	2 yrs.	Neg.	Normal	Neg.	Neg.	4 times	2 yrs.	Neg.	Neg.	+
13	A. 28194	R. K. June 30, '11	F. 22	Chronic splenitis	June 29, '12. Well	25x18x8 cm.	1530G	7 yrs.	Neg.	+1	Neg.	+1	Neg.	7 yrs.	Neg.	Neg.	+
14	A. 58017	E. J. J. Sept. 7, '11	F. 43	Chronic splenitis	Sept. 23, '12. Well	20x12x8 cm.	610G	20 yrs.	5 yrs. +	(Cirrhosis) Normal	Neg.	Neg.	Neg.	5 yrs. +	Up to age of 29	Neg.	Neg.
15	A. 58751	C. W. Sept. 26, '11	F. 25	Some areas of endothelial re-mains	Sept. 22, '12. Well	32x20x12 cm.	4500G	8 yrs.	6 wks.	Normal	Neg.	Neg.	Spit blood with menses	Neg.	Neg.	Neg.	Neg.
16	A. 65378	A. C. June 5, '12	F. 56	Chronic splenitis	July 16, '12. Improved	18x12x8 cm.	980G	6 mo. + 1 Neg.		Normal	Neg.	Neg.	Neg.	6 mos.	Neg.	Neg.	Neg.
17	A. 68783	A. J. S. June 18, '12	F. 37	Chronic splenitis	Nov. 12, '12. Well	20x12x9 cm.	890G	9 mos. (4 yrs.?)	Neg.	+2	Neg.	Neg.	Twice	9 mos.	Neg.	Neg.	Neg.
18	A. 69913	S. H. July 5, '12	M. 49	Chronic splenitis	Aug. 24, '12. Well	19x11x9 cm.	1000G	2 yrs. (3 yrs.?)	2 yrs.	+2 (No cirrhosis)	Neg.	+at onset	Neg.	6 mos.	As a boy	Neg.	Neg.

* For a discussion of the pathology see "The Pathology of Splenomegaly: A Study of the Operative and Autopsy Material from the Mayo Clinic (St. Mary's Hospital)," by L. B. Wilson. Surg. Gynecology, and Obstetrics, vol. xvi, 1913.

BLOOD FINDINGS IN EIGHTEEN CASES OF SPLENECTOMY FOR SPLENIC ANEMIA.

Cave No.	Time of count.	Hemo- globin.	Erythro- cytes.	Leuko- cytes.	Small lympho- cytes.	Large lympho- cytes.	Polymo- pho- clears.	Myelo- cytes.	Rosino- philes.	Raso- philes.	Tanals.	Normo- blasts.	Megalo- blasts.	Poikilo- cytosis.	Polychro- mato- philia.
1 (P3539)	2 days before operation.	%	4,501,000	1,600					%	%	%				
2 (G8869)	7 years after operation.	50	3,800,000	8,600											
3 (P7074)	80 days before operation.	70	5,200,000	4,800											
5	1 day before operation.	57	5,030,000	2,000											
4 (A9315)	1 yrs. 8 mos. after operation.	85	4,800,000	3,000											
2	2 weeks before operation.	40	4,600	4,600											
7	7 months after operation.	70	4,280,000	2,700											
3	3 weeks before operation.	50	2,900,000	5,000											
5 (A10324)	70 weeks before operation.	70	..	9,500	Smears negative			
6 (A18026)	3 weeks after operation.	82	..	34,800	4.0	..	93.0	..	3.0	Smears negative			
6	6 months before operation.	20	1,200,000	7,000	22.5	..	70.0	..	2.0	0.5	..				
2	2 days before operation.	47	3,300,000	2,500	17.5	7.0	73.0	..	1.5	0.5	0.5	..	+		
10	10 days after operation.	55	9,900	9,900	5.6	5.0	80.6	..	0.6	0.5	2.3	..			
7 (A20818)	45 weeks after operation.	45	3,740,000	12,400	6.0	8.0	85.5				
4	4 months after operation.	80	4,000,000	8,700											
3½	3½ years after operation.	90+	5,000,000	8,500	23.0	3.0	72.0	1.0	1.0				
2	2 weeks before operation.	60	4,640,000	7,700											
8 (A22020)	6 weeks after operation.	69	5,100,000	7,800	19.6	10.4	64.4	..	4.0	0.8	0.8				
4	4 weeks after operation.	73	3,060,000	11,000	12.3	1.3	80.6	..	3.3	2.0	0.3	..	2		
0 (A27414)	3 days before operation.	50	3,090,000	28,800	13.0	8.6	72.3	..	3.0	2.3	0.6	..			
1	1 month after operation.	95	5,600,000	10,500	7	2.5	79.0	4	7.5	1.0	0.6	1	..		
10 (A35431)	3 years after operation.	35	3,030,000	3,200	13.6	5.0	78.6	..	1.0	1.0	0.6	1	..		
2	2 months before operation.	69	4,600,000	3,400								Smears negative			
1	1 week before operation.	50	4,550,000	1,000	43.0	19.0	30.0	1	..	2.0	5.0	..			
11 (A39665)	12 days before operation.	73	4,330,000	3,350	35.5	21.0	37.5	..	4.0	1.0	1.0	..			
18	18 days after operation.	90	4,000,000	5,144								..			
6	6 years after operation.	65	5,420,000	3,750	16.5	8.5	73.5	..	1.0	2.3	0.5	..			
12 (A49050)	2 weeks after operation.	67	5,680,000	14,200	16.3	6.0	73.3	..	1.0	1.0	1.0	..			
2½	2½ years after operation.	80	4,960,000	11,750								..			
2	2 weeks before operation.	60	2,950,000	7,900	23.0	2.0	74.0	..	1.0	1.0			
13 (A25194)	2 weeks after operation.	85	4,800,000	9,200	15.0	4.5	76.0	..	3.0	1.5			
2	2 years after operation.	90	4,900,000	3,400	21.5	6.5	68.5	..	0.5	1.0	2.0	..			
14 (A58017)	3 days before operation.	89	4,820,000	7,200	26.5	8.0	64.0	..	0.5	..	1.0	..			
5	5 weeks after operation.	70	3,970,000	4,900	26.7	8.0	60.7	..	4.3	..	0.3	1			
15 (A58751)	2½ weeks before operation.	75	4,760,000	12,500	19.7	6.0	71.0	..	2.7	0.7			
1	1 year after operation.	100	4,800,000	15,000	Differential count	abn	normal	not				..			
16 (A68578)	2 days before operation.	50	4,200,000	5,100	13.0	2.0	78.0	..	3.3	2.7	1.0		
4	4 weeks after operation.	60	4,320,000	15,600	11.0	9.0	77.7	..	1.7	0.3	0.3	1	..		
55	55 days before operation.	70	4,600,000	2,700	19.4	8.0	70.0	..	2.0	..	0.6		
17 (A68788)	2 weeks after operation.	70	14,200	14,200									
5	5 months after operation.	88	4,800,000	10,800	46.7	2.3	45.3	..	1.3	2.0	2.3		
18 (A69913)	1 week before operation.	45	5,080,000	5,500	30.0	9.7	57.0	..	1.7	0.7	0.7		
3	3 months after operation.	90											

NOTE.—A differential count of 200 or 300 cells was made in these cases. All cases save numbers 4 and 15 gave histories suggesting the intermittent recurrence of anemia. Where many counts were made a representative section is given.

GROUP II. Infectious (?) splenomegaly (4 cases). Four cases of this series could not well be classified as splenic anemia. The histories were more or less complicated by the occurrence of other affections, suggesting that splenomegaly was not primary. It will be noted that 3 of the 4 patients eventually died, though there were no operative deaths. The division of these cases, as will be inferred from the histories, was made without any reference to the postoperative course. It is not my purpose to discuss these cases in detail, but rather to give their salient features in order that the evidence for excluding them from Group I may be clear. In many respects this small group of cases is the most interesting of the series.

CASE I (A34196).—J. E. G., male, aged fifty-five years. The chief complaint in this instance was of recurring attacks of upper abdominal pain of moderate severity. There was no history suggestive of ulcer and a clinical diagnosis of cholecystitis with splenomegaly was made. The enlargement of the spleen had not been noted before examination. There was nothing in the history which was suggestive of splenic anemia. At operation adhesions were found around the appendix, gall-bladder, and pylorus. The duodenum was bound to the pancreas and an ulcer may have been present. The spleen weighed only 320 grams and showed no connective-tissue hyperplasia. Splenectomy was the only operation performed, and the patient is in excellent health one and one-half years afterward.

CASE II (A59392).—W. P. D., female, aged thirty-seven years. For two years associated with three successive pregnancies there were similar attacks of illness, apparently without definite evidence of pelvic inflammatory disease. These attacks were characterized by the recurrence of severe chills and high fever, even to 105° and 106° , and upper abdominal pain of an indefinite nature. The last attack was the most severe and prolonged. During these attacks the spleen became very much enlarged. Examination and special tests were negative for malaria, syphilis, and tuberculosis. Blood cultures and examination of the blood for Leishmann-Donovan bodies were also negative. The patient's general condition was very poor as a result of her protracted illness. Hemoglobin, 70 per cent.; red blood cells, 4,060,000; white blood cells, 3100. Differential count was not abnormal. At operation evidence of widespread infection was found. There were adhesions in the pelvis, but particularly about the gall-bladder and common duct, was there evidence of old disease. The vessels of the spleen were brittle. The weight of the spleen was 640 grams, and pathologically the organ showed considerable increase in connective tissue. After operation the liver, which had been enlarged, became reduced to normal, and the symptoms abated somewhat. The patient gradually lost weight and strength, however, and died

four and a half months later with nephritis which may have been entirely a terminal condition. Anemia never became extreme. An autopsy was not obtained. In this instance the splenomegaly was doubtless part of a peculiar chronic infectious process.

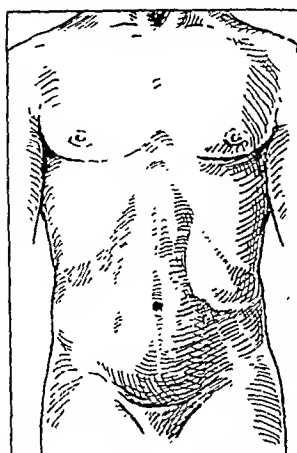
CASE III (A65749).—J. G., male, aged thirty-three years. This patient presented a rather complex history. What was probably a luetic sore had been present fourteen years before operation; the Wassermann reaction, however, was negative at the time of examination. Nine years and five months before operation hematemesis had occurred. The appearance of blood in the stool had been noted oftener than hematemesis, four times in the last three years. Splenomegaly had been present three years. The blood count was: Hemoglobin, 92 per cent.; red blood cells, 5,480,000; white blood cells, 7600. Differential not abnormal. The spleen extended to the level of the navel. Pathologically the spleen showed connective-tissue increase and infarcts. Its size was 21 x 15 x 7 cm. and its weight 900 grams. Death occurred two months after operation. At autopsy an acute nephritis, with cardiac dilatation, was found. In addition, tuberculous mediastinal and retroperitoneal lymphatic glands and a duodenal ulcer were discovered. Although the history in some respects suggested splenic anemia, in this case the pathologic findings prevent us from so classifying it. Hematemesis, which occurred before operation, may or may not have been due to bleeding ulcer.

CASE IV (A14838).—B. F. S., female, aged fifty-seven years. Raynaud's disease had been first diagnosticated five years before operation in this case and thyroidectomy for exophthalmic goitre had been performed four years previously. Rheumatoid arthritis had been present for three years. The spleen had been enlarged for three years, with rapid growth for six months, and at the time of operation it extended to the level of the anterior superior spine of the ileum. The blood count was: Hemoglobin, 84 per cent.; red blood cells, 5,600,000; white blood cells, 21,800. The differential count showed a polymorphonuclear leukocytosis of 93 per cent. At operation the spleen was found to measure 20 x 15 x 10 cm. and weighed 1340 grams. The patient also had gallstones, which it was thought should be removed later, and the liver was somewhat enlarged. A small piece of pancreas was ligated and cut away with the spleen. The patient died six weeks later, and at autopsy chronic nephritis and chronic general peritonitis were found.

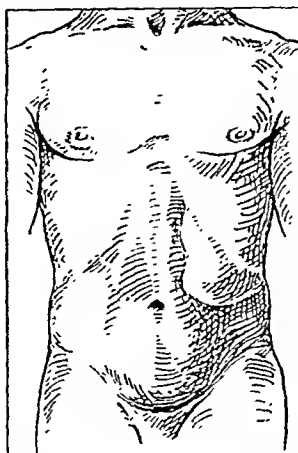
GROUP III. The remaining cases are grouped together for convenience: Wandering spleen, tuberculosis, cirrhosis of the liver, and pernicious anemia are considered.

(a) *Two Cases of Wandering Spleen.* Wandering spleen is, as a rule, readily diagnosticated if only the possibility of its occurrence be kept in mind. It has often been mistaken for movable

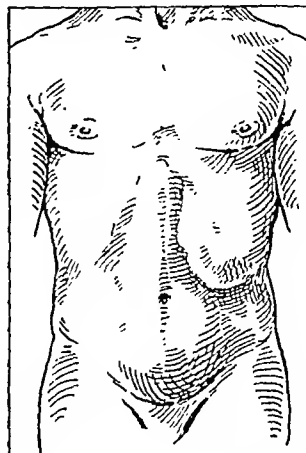
kidney. It has remained unrecognized when simple methods of exclusion and careful palpation would have decided the diagnosis definitely. One of these patients (A11038) was neurotic, but com-



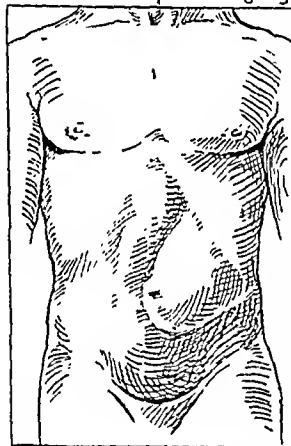
Case 1. A34496.
Infectious ? Splenomegaly.



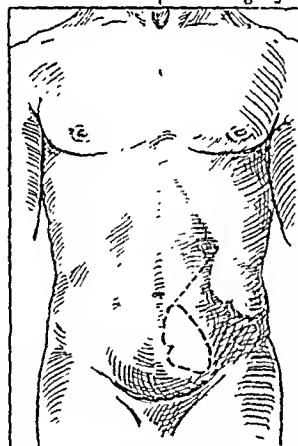
Case 2. A59392.
Infectious ? Splenomegaly.



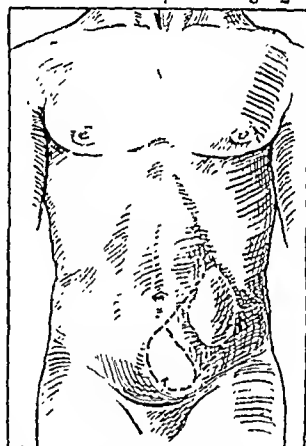
Case 3. A65749.
Infectious ? Splenomegaly.



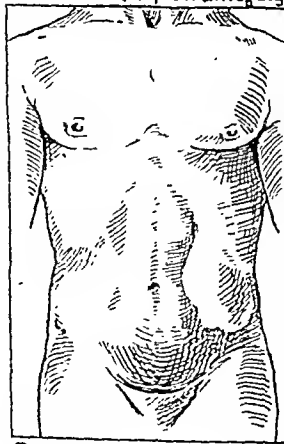
Case 4. A14838.
Infectious ? Splenomegaly.



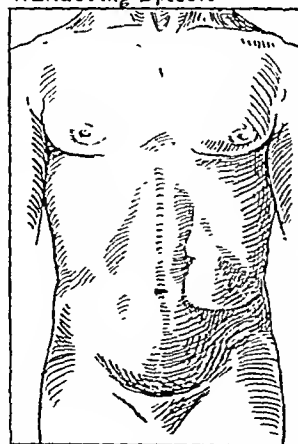
Case 1. A11038.
Wandering Spleen.



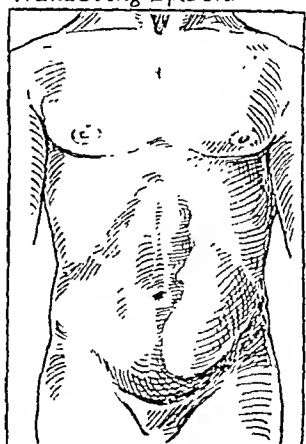
Case 2. A62258.
Wandering Spleen.



Case 1. G617.
Tuberculosis.



Case 1. A64259.
Cirrhosis of Liver.



Case 1. A7074.
Atypical Anemia.

FIG. 3.—Contour and position of spleen as observed clinically before operation.

plained of pain over the spleen to a degree which seemed to warrant splenectomy. A moderate grade of anemia was present. Four years after operation the patient's blood count is normal, though she complains of many neurotic symptoms. The second patient (A62258) had complained of recurring attacks of pain of an hour's duration for a period of four years. At operation a twisted pedicle was found, while the spleen could be moved to the lower abdomen and to the right of the median line, though it lay naturally opposite the navel. This patient is well.

(b) *One Case of Tuberculosis of the Spleen* (G617). Multiple abscesses and tuberculous deposits studded the organ, giving the appearance so commonly seen in the kidney. The length of the history had been sixteen months, and no definite evidence of tuberculosis was found elsewhere in the body before operation. The patient died four months later, however, with evidences of a disseminated tuberculosis. An autopsy was not obtained.

(c) *One Instance where Cirrhosis of the Liver Seemed to be Primary* (A64259). Although the patient was only twenty years of age, all parts of the liver were covered with contracted areas, while in volume the organ was increased. It was the opinion of the surgeon (W. J. Mayo) that the cirrhosis was primary. The weight of the spleen was 750 grams, and there was nothing in the pathology which indicated lues. This patient gave a history of splenomegaly for one year and recurrent anemia for two years. The blood count showed a secondary type of anemia, with a hemoglobin of 58 per cent. The leukocyte count was 4200. The patient developed ascites, and died two months after operation. An autopsy was not obtained.

(d) *One Case of Pernicious Anemia (?)* (A7074). In this instance the hemoglobin was low (45 per cent.), the color index was high, but less than one, and a few normoblasts and megaloblasts were found in the smears. After operation, however, a shower of normoblasts and megaloblasts occurred. The spleen extended below the navel and weighed 1640 grams. The patient, two and a half years after operation, states that he is weak and anemic, and unable to work, and a review of the case suggests the diagnosis of an atypical pernicious anemia. It has been impossible, however, to obtain a recent blood count, and the diagnosis at best remains very uncertain.

STATISTICAL SUMMARY.

Total number of splenectomies	27
Operative deaths	2 (7.4 per cent.)
Group 1. Splenic anemia.	
Well from six months to seven years (longer than one year, 10) . . .	12
Improved (1, blood normal, myocardial and renal insufficiency; 1 operated on six months ago)	2
Improvement several months, death three years after operation (hepatic cirrhosis?)	1
Death two and one-half years after operation, cause unknown . . .	1
Operative deaths	2—18

Banti's syndrome (included above).	
Operative death	1
Well (seven years, three and one-half years, one and one-half years, six months)	4—5
Spleens showing chiefly connective-tissue hyperplasia	13
Spleens showing lymphocytic hyperplasia	2
Spleens showing endothelial hyperplasia (Weichselbaum or Gaucher type)	3
Group II.	
Infectious (?) secondary splenomegaly.	
Well	1
Died from two to six months	3—4
Group III. Miscellaneous.	
Wandering spleens, well	2
Tuberculosis, death in four months	1
Atypical anemia (?), unimproved two and one-half years	1
Cirrhosis of liver, death in two months (ascites)	1—5

A consideration of this series of cases, in which splenectomy was done, impresses one with the fact that a proper grouping of conditions, in which marked enlargement of the spleen is associated, with an anemia of the secondary type is extremely difficult if not impossible at the present time. The clinical features form the best basis for a tentative classification, and especially assist us in recognizing clear-cut and uncomplicated cases of splenic anemia. The pathology of splenic anemia and those conditions which simulate it is too little understood, and conclusions for the present would best be drawn only from those reported cases in which pathological as well as clinical evidence has been published.

This review may also have indicated a possible relationship between gall-bladder disease and splenomegaly. It seems to have indicated more clearly, however, that there is a clinical syndrome conforming to the general conception of splenic anemia in which splenectomy is followed by a return to excellent health in a large percentage of cases, but in those instances in which the diagnosis is complicated by other diseases of a chronic infectious nature, the value of splenectomy is questionable.

It is necessary in these as it is in other medicosurgical conditions for the physician to learn the details of surgical prognosis. Splenectomy should be advised only after careful diagnosis, not only of the abdominal enlargement itself but also of the patient's general condition, and after the elimination of the existence of serious complications.

NOTE.—The reader is referred to the following articles: "Principles Underlying Surgery of the Spleen, with a Report of Ten Splenectomies," by W. J. Mayo, *Jour. Amer. Med. Assoc.*, January 1, 1910; "Surgery of the Spleen," by W. J. Mayo, *Surg., Gyn., and Obst.*, xvi, 1913; "The Pathology of Splenomegaly: A Study of the Operative and Autopsy Material from the Mayo Clinic (St. Mary's Hospital)," by L. B. Wilson, *Surg., Gyn., and Obst.*, xvi, 1913.

The author is indebted to H. G. Wood and A. Archibald for their assistance in compiling statistical data of the cases reported.

THE ADMINISTRATION OF OX BILE IN THE TREATMENT OF HYPERACIDITY AND OF GASTRIC AND DUODENAL ULCER.

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THE value of internal therapeutic measures is so difficult of conclusive proof that the following suggestion is offered with some hesitation. Yet in view of the strength of the physiological and pharmacological facts upon which the theoretical considerations have been based, and from the practical results obtained in some fifty preliminary cases, it is felt that the matter deserves publication in the hope that its worth may be tested by other physicians.

Our knowledge of the physiology of the stomach, particularly in regard to the functions of the pylorus, has in recent years made great advances. Clinicians, however, have been slow to attempt to utilize the new knowledge of normal physiology to shed light upon the pathological physiology of clinical disorders. This may be due in part to the widespread spirit of pessimism with which the subject of the medical diseases of the stomach is so commonly regarded; for this chapter in the recent history of internal medicine has not been a bright one. Our power to furnish relief in cases complaining of dyspepsia has remained far from satisfactory. For the purpose of determining treatment that can be recommended with confidence that improvement will result, the study of the stomach contents has not justified the hopes that were formerly held. In the diagnosis of pyloric stenosis, it is true, the examination of the gastric contents is of great importance, and some assistance is obtained in questions of carcinoma; but in the diagnosis of the functional diseases, and even of gastric and of duodenal ulcer, the aid obtained by means of test meals is so slight as hardly to justify the trouble to the examiner and the discomfort to the patient. For purposes of classification of cases investigation of gastric contents has led to the recognition of certain abnormalities of function, such as hyperacidity, hypersecretion, etc.; but even in these no complete explanation of the symptoms has been reached, and over them but little therapeutic control has been gained. A complete reconsideration of the subject without bias from previous clinical teachings is therefore desirable.

In common clinical experience the most frequent form of dyspepsia is that characterized by "sour stomach" and "heart-burn," or pain after eating. Cases of this are seen almost daily in every large clinic. They are commonly regarded as cases of hyperacidity, but while many of them do show hyperacidity in the test breakfast

withdrawn after an hour in many others the contents are not abnormal. The surgical findings of late years have shown that many of the more severe of these cases have gastric or duodenal ulcers, but it is still too advanced a view to maintain that ulcer is present in all. Thus in routine practice an uncertain diagnosis is made of hyperacidity or ulcer. In treatment the patient is given directions and diet according to the physician's opinions, and an alkali to be taken for palliation as necessary; but in many cases no appreciable improvement results.

This state of affairs is not an inspiring one, yet we must face the fact that with the best intentions in the world and with many new resources at our command it has been hardly possible to advance our power to benefit these cases beyond that of the physicians of past generations, unless we yield to the demands of the surgeons and consent to exploratory laparotomies by wholesale. Present methods of clinical examination have failed us beyond a certain limited extent, and have left us still to wait for new developments. But rather than wait passively for new power to come to us it is our duty to search constantly for ways around the difficulties which we cannot surmount, and to follow any new paths still unexplored, however slight their promise may seem.

Instead of sifting objective evidence let us consider for a moment in detail the subjective sensations as described by the more intelligent patient through a sample day. He rises and goes to breakfast without symptoms. He eats his breakfast and other meals with relish, but with well-justified apprehension; he leaves the table still without discomfort, but within a short time he becomes conscious of a burning sensation, as from a chemical irritant clearly referred to the same point to which hot fluids ingested by the mouth can be traced, unquestionably to the stomach. The discomfort gradually increases; belching and acid regurgitation may occur. Then after an hour or more of suffering the symptoms gradually pass off, only to recur after the next meal.

Now in all this process there is one point which is to be noted above all others. This is that through it all the patient's one longing is that the stomach may become emptied of its contents as soon as possible. Many patients are conscious that vomiting will give relief, and induce it for that purpose; but more, while no less conscious that evacuation of the stomach is to be wished for, simply endure the distress as best they can until the meal has passed through the pylorus. The association in the mind of the intelligent dyspeptic between an empty stomach and relief is an invariable one. Can we not therefore take the hint and consider whether the cause of symptoms may not be a disorder of the normal function by which the stomach discharges its acid contents into the duodenum through the pylorus?

Let us therefore review the physiology of the pylorus to see if there

is any way in which its action may with any likelihood be disturbed so as to interfere with the prompt passage of gastric contents of normal or increased acidity through its opening. According to Cannon¹ the control of the pyloric sphincter depends upon two factors. The signal for the first opening is the appearance of free acidity on its gastric side. This allows a jet of acid chyme to enter the duodenum. The presence of acid in the duodenum, however, is a signal for the closure of the pylorus, which continues to act until this acid in the duodenum is neutralized, after which if the contents before the pylorus are still acid the sphincter may relax again and repeat the process. But so long as the contents of the duodenum are acid the pylorus cannot open, no matter how high may be the acidity on its gastric side. For the proper functioning of the pylorus, therefore, it is necessary to have a proper balance between acid secretion on the part of the stomach and acid-neutralizing power in the duodenum. While the periodic opening of the pylorus will be delayed if gastric acidity is deficient, it will also be delayed if the neutralizing fluids in the duodenum are deficient. Now we know that in the cases which we have been considering the gastric acidity is at least normal and is often increased. May it not be that it is the neutralizing power of the fluids in the duodenum that is at fault, unduly prolonging the period during which the acid secretion of the stomach accumulates before the pylorus awaiting its discharge?

The neutralization in the duodenum of acid contents received from the stomach is effected by the bile and by the pancreatic juice, as well as by secretion of the duodenal mucosa described by Pilcher.² While the amount of the second and the third of these cannot be influenced, the flow of bile, as shown by Pfaaf and Balch,³ can easily be increased by the administration by mouth of ox bile. Thus since the possibility that so-called hyperacidity and even gastric duodenal ulcer may owe their symptoms to delayed neutralization of duodenal contents is not beyond the range of the imagination, and since if present such delayed neutralization should theoretically be corrected by the administration of ox bile, a series of cases with symptoms of these conditions has been treated in this way as a therapeutic experiment.

The clinical test thus undertaken comprises somewhat over fifty cases, which can be regarded as typical of the class formerly considered as hyperacidity, but now after the teachings of Moynihan and Mayo under the suspicion of chronic gastric and duodenal ulcer. The clinical histories are not individually of such interest that detailed description is desirable. Their most prominent symptoms were pain and pyrosis following the ingestion of food

¹ The Mechanical Factors of Digestion, 1911.

² AMER. JOUR. MED. SCI., 1911, cxlii, 687.

³ Jour. Exper. Med., ii, 49.

after a more or less definite interval and relieved temporarily by sodium bicarbonate. Vomiting occurred occasionally in a minority of the cases, and when it occurred invariably gave relief, so that some frequently induced vomiting to stop the pain. In four cases there was a clear history of more or less recent hematemesis. In one case an x-ray examination showed the appearance of an extensive gastric ulcer. In two cases ulcer had been demonstrated at operations. The great majority were office and out-patient cases, whose daily habits continued unchanged during observation.

The treatment was as follows: A general diet list was given merely to avoid clearly unsuitable foods; this was regarded by the experienced patients as a generous one. A caution against overeating was given, and stress was laid upon thorough mastication to insure prompt action upon the food by the gastric juice. The ox bile was given in pills prepared by a Boston pharmacist according to the directions of Pfaff,⁴ each containing 0.25 gram of dried and pulverized ox bile, salol coated to conceal the taste and to prevent dissolution in the stomach. Two or three of these pills were given after meals three times a day for a week, after which, as a rule, the number was reduced. In some instances where the appetite was not good, or where there was other reason to suspect that the gastric secretion was not always active, dilute hydrochloric acid and tincture of nux vomica, of each eight minims, were given in water before meals, and for temporary relief sodium bicarbonate and milk of magnesia were recommended to the few patients not already familiar with them. Aside from these measures, and laxatives when needed for constipation, the daily life of the ambulatory patients continued as before, and in the less numerous cases in bed on account of hematemesis or other severe symptoms as little other treatment was given as possible.

The results of this treatment were such as to lead the author to the belief that they could not be explained by the general directions given, but must be laid to the influence of the bile. In practically all cases followed the patients described a satisfactory improvement beginning within a few days, and at the end of a week or ten days gave a highly favorable report of their condition. The seven cases in which from hematemesis or other special evidence the presence of ulcer was undoubted are too few, it is true, from which to draw final conclusions; yet with one possible partial exception their course was no less favorable than that of the less serious cases. The four with a history of vomiting blood all promptly became free from symptoms, although two of them refused to give up their work, and were therefore treated as ambulatory cases. The patient whose x-ray plates gave the appearance of ulcer became free from pyrosis and pain, although some feelings of distress,

⁴ Loc. cit.

possibly neurotic, persisted. Of the cases with ulcers demonstrated at operation the following brief descriptions may be given: The first was a woman in whom during an operation for fibroid a pyloric ulcer was found. She had for many years had daily attacks of pain after eating so severe that she frequently induced vomiting for their relief. Under the ox bile treatment she rapidly improved, but in spite of this a gastro-enterostomy previously determined upon by the surgeon was performed. The other case had had a gastro-enterostomy performed for a demonstrated duodenal ulcer in 1908. In 1910, at a second operation, a deep ulcer was found in the jejunum opposite the stoma, which was resected with obliteration of the gastro-enterostomy. Hardly had he recovered from this second operation when symptoms returned. The bile treatment was then instituted and he became free from symptoms for a year. At the end of that time, however, he reported that the pains had recurred and that he had taken the pills which he still had without relief. A prescription for some fresh pills was given him, and he did not return. On account of a change of residence he could not be traced, so that the outcome is uncertain.

But it is not the purpose of this paper to advocate the use of ox bile as the sole treatment of gastric and duodenal ulcer. It is in cases of dyspepsia of a milder type in which even bed treatment is not considered necessary that the treatment is most clearly supported by its results. In no typical instance among the cases followed has pyrosis and pain directly connected with eating failed to be relieved; in two apparent exceptions it turned out that the patients had not had the prescription filled. In one somewhat atypical patient, to whom, however, the treatment was given, no benefit was obtained; he later showed marked improvement and gain in weight under antisyphilitic treatment. Still later he drifted into the hands of a surgeon who explored him, but was unable to find any organic lesion. Cases in neurotic persons were somewhat less constantly entirely relieved, but many extremely neurotic patients were enthusiastic over the benefit received. In a word, from the experience of the past two years dyspeptics of the so-called hyperacidity type, which were formerly treated with very indifferent success, have when treated in the same way but with in addition the use of salol-coated ox-bile pills seemed to obtain relief. It is therefore hoped that in the hands of others the treatment may prove no less successful.

SUMMARY. There is reason to suspect that in hyperacidity and in gastric and duodenal ulcer the symptoms are at least in part due to delay in the neutralization of the acid contents discharged into the duodenum. The administration of ox-bile pills (salol coated) by the mouth should theoretically correct this fault. Empirically such administration of ox-bile has seemed to be of service in the relief of pyrosis and pain after eating; it has been followed by improvement in cases of gastric and of duodenal ulcer.

In conclusion, it must be stated that if the method here described proves of value the chief credit is due to the teachings of Cannon and of Pfaff, of which it is but a practical application.

NOTE.—While the proof-sheets of this article were in hand a third patient, omitted by oversight from this group, called for advice in an acute respiratory infection. In February, 1911, at operation for gallstones, a duodenal ulcer was found, and on his leaving the hospital the ox-bile treatment was given. Since then he has not had to consider his digestion except to take an occasional dose of sodium bicarbonate after indiscretions in diet.

OBSERVATIONS ON THE INTESTINAL BACTERIA IN PELLAGRA.¹

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(From the Laboratories of the New York Post-Graduate Medical School and Hospital.)

A GENERAL survey of the fecal bacteria in pellagra was undertaken in 1910 and 1911 by the Illinois State Pellagra Commission. A brief summary of that work has been published² and the detailed record of the work has also recently appeared.³ In general it was ascertained that the fecal bacteria in pellagra, when examined directly with the microscope, are different from the normal in their quantitative relationships, and that unusual kinds of bacteria, more or less heterogeneous in nature, are present. The cultural tests also brought to development unusual quantities of certain normal types, *Bacillus bifidus*, *Bacillus welchii*, and micrococci, in some cases, as well as a considerable variety of bacterial forms not ordinarily found in the feces of healthy men. None of these changes appeared to be constant. During the acute attack accompanied by diarrhea the Gram-positive cocci were nearly always abnormally numerous, and the Gram-negative bacilli were less numerous than normal in these cases. These changes were also observed in the subacute cases and even persisted to a slight degree after recovery from the skin lesions. The percentage of these cocci and bacilli are indicated in Chart I, along with data of similar observations on healthy men⁴ for comparison. These changes,

¹ This paper forms a part of the progress report of the Thompson-McFadden Pellagra Commission of the New York Post-Graduate Medical School.

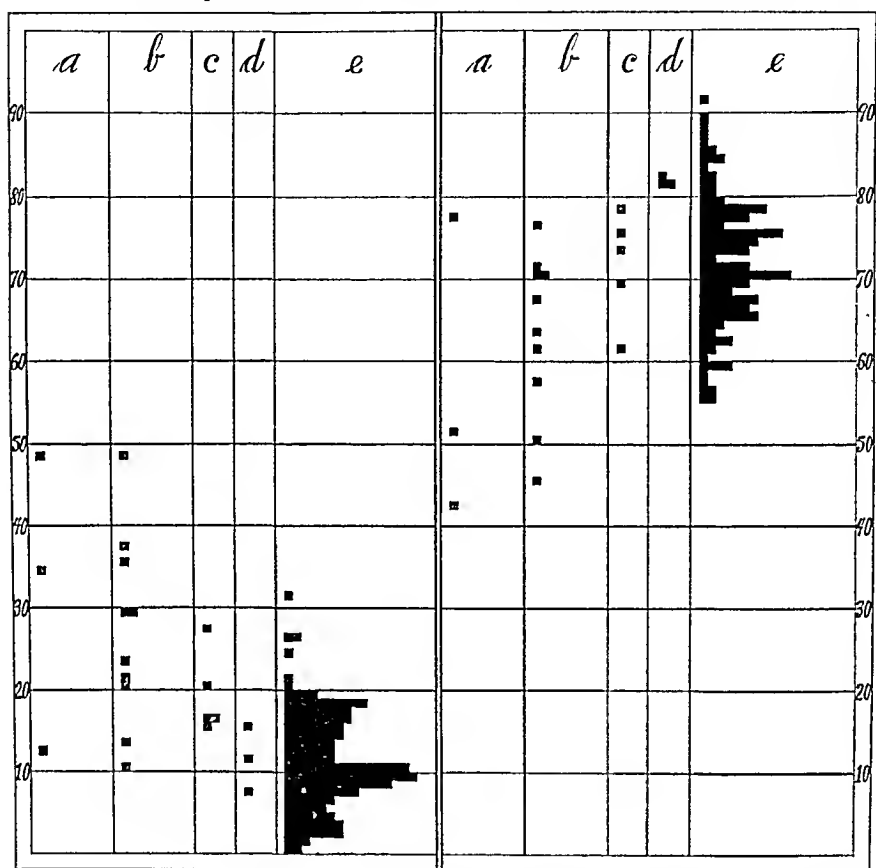
² Pellagra in Illinois, Arch. Int. Med., August and September, 1912, x, 123 to 168, 219 to 249.

³ Report of the Pellagra Commission of the State of Illinois, Springfield, Illinois, 1912.

⁴ Jour. Infect. Dis., April, 1909, vi, 123 to 169.

which were nearly constant, were such as might be expected as a natural result of the digestive derangement. There was no indication of a substitution of the normal intestinal bacteria by an abnormal invader. The abnormal types were various in nature and in no case dominant in numbers.

CHART 1.—Percentage of gram-positive cocci and of Gram-negative bacilli in the feces.
Gram-positive cocci. Gram-negative bacilli.



Percentage of Gram-positive micrococci and of Gram-negative bacilli in the feces: (a) three examinations in acute pellagra; (b) ten examinations in subacute pellagra; (c) four examinations after recent recovery from pellagra; (d) three examinations in insane individuals not pellagrins; (e) one hundred and thirty-seven examinations in healthy men. The data for a, b, c, and d are taken from MacNeal, Allison, and York, Report of the Pellagra Commission of the State of Illinois, Springfield, 1912, pp. 55 to 160, and the data for e from MacNeal, Latzer, and Kerr, the Faecal Bacteria of Healthy Men, Jour. Infect. Dis., 1909, vi, 123 to 169.

During the course of the primary examinations subcultures were made from a number of colonies and preserved for subsequent study. One hundred of these bacterial strains were subjected to agglutination tests, using the blood serum from cases of pellagra and from normal individuals. Three of the one hundred strains reacted in a somewhat suggestive manner. These were strains Nos. 14, 35, and 67. All were derived from cases of pellagra at

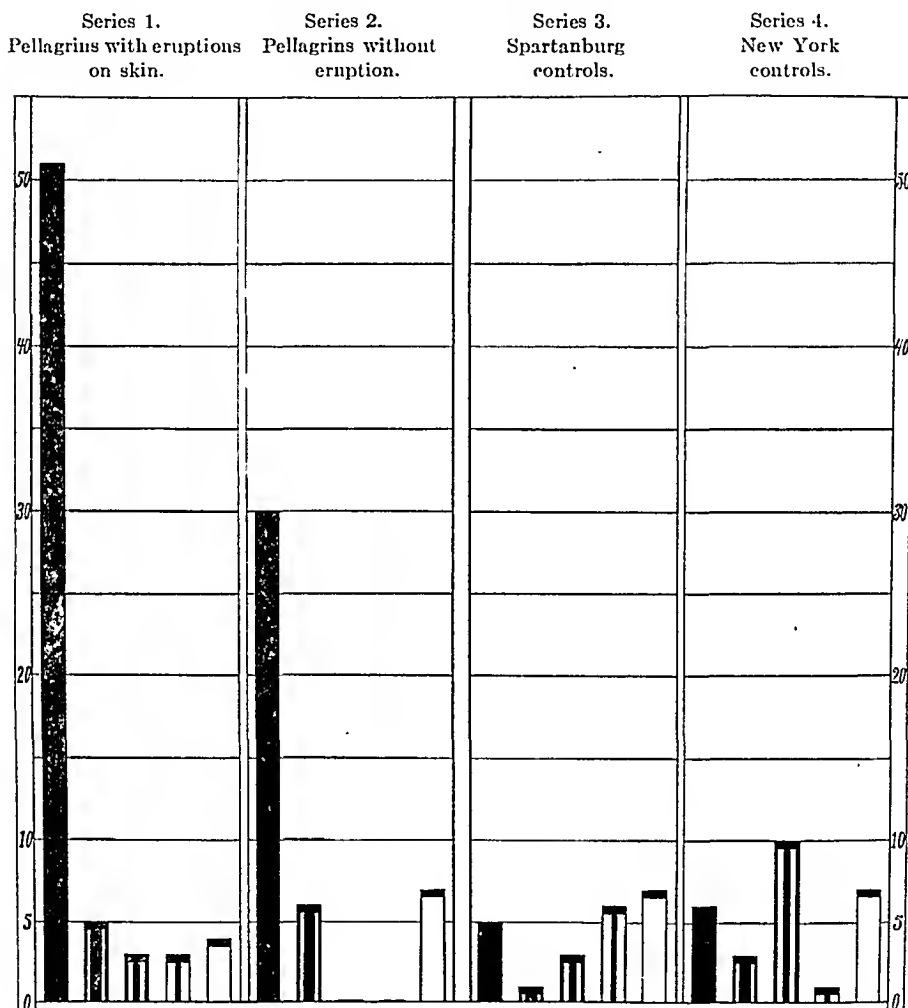
Peoria, Illinois. They were agglutinated by sera of pellagrins at Peoria, at Kankakee, and at Chicago. The suggestion of a specific relationship to the disease was considerably weakened by the fact that these bacteria were also agglutinated by the sera of insane patients, not pellagrins, at Peoria and at Kankakee, and by the sera of apparently normal persons at Kankakee, Chicago, and Urbana, Illinois. Two of these bacterial strains, Nos. 14 and 67, appear to be identical in nature. The organism is a short rod about $4.0\ \mu$ long by $1.4\ \mu$ thick on the average. The size is variable, however, variations in length from 2.4 to $6.2\ \mu$, and in thickness from 1.0 to $1.6\ \mu$ being observed in young vigorous cultures. Gelatin is not liquefied. In litmus milk the organism grows without producing an acid reaction. There is slight coagulation after four days and a slow digestion of the casein. No gas is produced in broth containing dextrose, levulose, lactose, saccharose, or maltose. Fresh cultures on agar are colorless, but later assume an orange color, and this production of pigment seems to become more pronounced with continued artificial culture. Strains Nos. 14 and 67 agree in all these characters, and strain No. 35 in all except the pigment production. It has remained colorless. Inoculation of animals (guinea-pigs, rabbits, and monkeys) has been followed by loss of weight, but has not resulted in the death of any animal.

Further study along these lines has been undertaken by the Thompson-McFadden Pellagra Commission at the New York Post-Graduate Medical School during the summer of 1912. The opportunity was here presented to test this culture against the sera of pellagrins from a different part of the country, South Carolina. These recent cases have been divided into four series: First, 66 pellagrins showing lesions on the skin at the time the blood was taken; second, 43 pellagrins who did not show an eruption at the time but in whom a reliable history of the disease was obtained; third, 22 individuals living in the pellagrous district, Spartanburg County, South Carolina, but free from any sign or definite history of the disease; fourth, 27 individuals in New York, including clinic patients and some physicians who kindly furnished their own blood for this work. The agglutination tests were performed by the macroscopic method, a suspension of the bacteria in salt solution being mixed with an equal volume of a 20 per cent. solution of the serum in a small tube for each test, the final dilution of the serum being one part in ten. It was incubated for an hour and the progress of events recorded at intervals of fifteen minutes. Complete clumping and precipitation of the bacteria to the bottom of the tube was recorded as a complete reaction. Grades of almost complete, marked, slight, and negative were also distinguished. The results are shown graphically in Chart II.

Of the 66 sera in the first series, from pellagrins with the skin

eruption, 51 gave complete agglutination, 5 almost complete, 3 slight, and 4 negative reactions. The 43 sera of the second series gave reactions distributed as follows: complete 30, almost complete 6, marked none, slight none, negative 7. Of the whole 109 different sera from pellagrins, 74.3 per cent. gave complete agglu-

CHART II.—Results of agglutination tests.



Results of the agglutination tests. Complete reactions (1) in solid black at the left in each series; then in order (2) almost complete, (3) marked, (4) slight, and (5) negative reactions.

tionation, 10.1 per cent. almost complete, 2.7 per cent. marked, 2.8 per cent. slight, and 10.1 per cent. negative reactions. The 22 sera of the third series, non-pellagrins of South Carolina, gave 5 complete agglutinations, 1 almost complete, 3 marked, 6 slight, and 7 negative reactions. The 27 New York controls gave 6 complete agglutinations, 3 almost complete, 10 marked, 1 slight, and

7 negative reactions. Of the total 49 controls, 22.5 per cent. gave complete agglutination, 8.2 per cent. almost complete, 26.5 per cent. marked, 14.3 per cent. slight, and 28.5 per cent. negative results. These findings are obviously not sufficiently clear-cut to warrant the assumption of a specific agglutination reaction of this bacterium with the serum of pellagrins, and yet they are such as to stimulate further work along this line.

The conservatism of this statement is not due to the fact that we have employed serum dilutions of one in ten instead of higher dilutions, for many of these positive sera have been tested in higher dilutions, up to one in four hundred, and have produced definite agglutination in such strength. The suggestion of specificity is, however, seriously opposed by the fact that sera from apparently normal individuals give precisely parallel results in some instances.

We have attempted to employ the complement-fixation test on a number of sera, using an antigen prepared from a culture of strain No. 67. Positive results have been obtained in a few cases, but it has not been possible to try it in a sufficient number of cases to determine the value of the test. We are also attempting to perfect a precipitin test. We hope that it may be possible, by employing these in conjunction with the agglutination test, to obtain more decisive results during the coming pellagra season.

A few cutaneous and intracutaneous tests on patients were performed during the year of 1912, using a vaccine made from a culture of strain No. 67. Of the 9 patients to whom the cutaneous test was applied, 1 gave a moderate reaction, 3 a slight reaction, and 5 were negative. The intracutaneous test on the same 9 patients gave a marked reaction in 1; a marked and a moderate reaction in another case in 2 tests; a slight reaction in 3 cases; a slight reaction and a negative reaction in another case in 2 tests; and a negative reaction in the 3 remaining cases; 2 controls gave negative results, one of them in two tests. The behavior of the cases, especially those on whom the test was repeated, seemed to suggest a difference in the reaction according to the stage of the disease, but the cases tested are still too few to bear analysis along this line.

While these various experiments with this culture were in progress we have undertaken to isolate further bacterial strains from the intestinal contents of pellagrins brought to New York for study. These cultures have been isolated by the methods previously employed, more especially by plating on blood-agar and ascitic-fluid-agar, from the feces, and also from the intestinal juice obtained through the Einhorn duodenal tube; 693 new bacterial strains were isolated in this way during 1912, and these have been tested against sera of pellagrins and others in approximately 2000 agglutination tests. This work is not yet completed, but it seems certain that we have failed to isolate any germ similar

to strain No. 67 from the feces of these new cases. From the duodenal fluid, however, a few strains have been obtained which have given positive agglutination tests with the serum of cases of pellagra, and which seem to agree in their biologic characters, so far as they have been tested, with strain No. 67.

It is evident that this phase of the investigation is in an unfinished condition, and we do not wish to draw any definite conclusions at this time. This report will give an idea of one of the avenues along which we have approached the possible bacteriologic phase of the problem of pellagra, and indicates one of the lines we hope to follow during the present year.

THE RATIONAL TREATMENT OF TETANUS, WITH A REPORT OF TWENTY-THREE CASES FROM THE EPISCOPAL HOSPITAL, PHILADELPHIA.¹

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THIS paper is written with three purposes: (1) To report 23 consecutive cases of tetanus treated at the Episcopal Hospital, Philadelphia, during the last eight years; (2) by a review of the recent literature to endeavor to inculcate rational methods of treatment; and (3) in the hope that others may profit by our mistakes, as we have profited ourselves. For permission to record these case histories, as well as for the privilege of having under our personal care 11 of the patients, we desire to express our cordial thanks to the various members of the staff in whose services the patients were treated.

It is necessary first of all to inquire whether there is any such thing as a rational treatment for tetanus. We hold that treatment can be rational only when it is founded on a knowledge of the pathogenesis of the disease in question; and we believe that in the case of tetanus such knowledge exists.

Though previous generations had enough clinical acumen to class tetanus among diseases of the nervous system, and though the discovery of the *Bacillus tetani* by Nicolaier in 1884, and its isolation in pure culture by Kitasato in 1889, proved it to be an

¹ Read at a meeting of the Episcopal Hospital Clinical Society, November 18, 1912.

infectious disease, yet it is only within the past ten years that any definite knowledge as to its pathogenesis has been acquired. This knowledge has been secured almost solely through animal experimentation, and it is only as a result of the information gained in this way that rational treatment has become possible. Previous treatment, even if successful, was purely empirical. Especially noteworthy in the development of our knowledge have been the elaborate researches of Marie and Morax (1902), Meyer and Ransom (1903), Sawamura (1909), and v. Graff (1912). We have drawn freely from the various publications of these authors, as well as from Frazier's excellent critical review of the subject.

It is known that the disease is a pure toxemia. The bacilli or their spores may exist indefinitely in the tissues, and *no symptoms will be produced unless toxins are formed*. If the toxin is introduced into the system, it produces all the characteristic symptoms of tetanus even though no bacilli are present.

EXPERIMENTAL TETANUS. *Tetanus Ascendens.* In the small animals used in laboratory work the symptoms of the disease almost always begin in the inoculated extremity (*local tetanus*), and though other neighboring parts may become affected subsequently, yet trismus and retraction of the head almost never are observed, the disease being terminated by death or recovery before this stage is reached. In such animals (rabbits, rats, mice, frogs) if one lower extremity is inoculated with tetanus toxin the symptoms develop first and are most pronounced in that extremity; the opposite lower extremity is involved later, but not to the same extent; and when the spinal muscles become affected those of the injured side frequently are more involved than those of the uninjured side, thus resulting in pleurothotonos. The disease in such cases is known as Tetanus Ascendens; its symptoms develop first in the injured part and gradually ascend.

Tetanus Descendens. Usually in the larger animals and in man, in whom the disease is acquired not by the injection of toxin but by inoculation of the bacilli of tetanus, the symptoms begin first in the muscles of the neck and jaws, *no matter where the point of inoculation*. Subsequently the muscles of the back and trunk are affected, and finally those of the extremities, especially the lower extremities. The disease in these cases is distinguished as Tetanus Descendens. In man ascending tetanus is not extremely rare (Cases 2 and 4 of our series), though the initial symptoms (cramps and stiffness in the wounded extremity) often are overlooked, and the case is classed as one of pure descending tetanus. Mixed forms also exist, in which the disease seems to run both an ascending and a descending course.

Is there a satisfactory explanation for the difference between these two forms of tetanus, ascending and descending—the former being that which is produced experimentally, and the latter that which

occurs in nature? Zupnik in 1900 found that he could produce descending tetanus experimentally, even in small animals, provided the toxin was injected into muscle-free parts of the body, such as the tips of the toes (rabbits). These results were confirmed in 1909 by Sawamura, and it was he who advanced the true explanation for the difference between tetanus experimentally produced and that which occurs in nature. In experimental animals the toxin always had been injected into the muscular parts (usually the thigh or calf of the leg), and here it came into relation almost immediately with the motor nerves, was absorbed rapidly by them, and the part of the spinal cord first to be affected was that in anatomical relation with the wounded limb. In man, however, the usual point of inoculation is the hand or foot, and while a certain amount (perhaps a large amount) of toxin eventually reaches the nearest motor nerves and ascends them to the spinal cord, yet other portions of the toxin are taken up first by the lymphatics, then enter the general circulation, and passing out from the left heart are carried in short order to *the end-plates of all motor nerves throughout the body*. The portions of toxin reaching in this way the end-plates of such short nerves as those of the facial, cervical, and spinal muscles will reach the spinal cord through these short nerves, and will begin to produce tetanic spasm in the parts supplied by these short nerves, even before the toxin in the wounded extremity has had time to ascend the nerves of that extremity as far as the anatomically related region of the spinal cord. In this way, therefore, descending tetanus is to be explained. And Sawamura found that among 23 reported cases of ascending tetanus in man the point of inoculation was in a muscular part in every case but one, thus strengthening his view that the occurrence of ascending tetanus is due to the ready access of the toxin to the motor nerves. To prove this supposition still farther, he showed experimentally that if the nerves of an extremity are divided no local (ascending) tetanus can be produced by the injection of toxin; and that even if descending tetanus finally develops after many times the usual lethal dose of toxin has been injected, yet no local tetanus occurs in the enervated extremity.

Cephalic tetanus, as seen in man following wounds of the head or face, is to be explained in this way: It is a local tetanus, and it occurs first in the wounded part, and is manifested first by facial spasms and paralysis, because the toxin finds ready access to the short cranial nerves and reaches the centres which control them long before the toxin admitted to the general circulation reaches the spinal cord through other, longer nerve trunks.

PATHOGENESIS OF TETANUS. 1. *The toxin ascends the peripheral nerves to the spinal cord.* From what has been said above it is evident that the symptoms of tetanus are due to the action of the toxin on the central nervous system, especially to its action on the

spinal cord. It was shown by Marie and Morax in 1902, by Meyer and Ransom in 1903, and has been repeatedly demonstrated by experimenters since their time, and it may be accepted as irrefutably proved, that in ascending tetanus the toxin ascends the nerves of the wounded part (especially the motor nerves) until it reaches the spinal cord; that only when it reaches the cord does it begin to produce symptoms; that the first symptoms produced are in the parts supplied by the portion of the cord first attacked; that the toxin spreads in the cord, up or down, more especially ascending it; and that it produces symptoms in the parts supplied by every portion of the cord attacked. It is known that tetanus toxin can and does exist free in other portions of the body, such as the internal organs (liver, spleen), where it may be found after death; but that only those portions of the toxin which reach the spinal cord are able to produce recognizable symptoms.² And it is known that after death little or no toxin can be found in the spinal cord. At first sight this seems paradoxical, but the explanation is that when the toxin reaches the cord it soon enters into combination with the nerve tissue, becomes impregnably entrenched there, and cannot be dislodged by any known methods.

The peripheral nerves have little power of neutralizing the toxin—no more power than has the liver, for instance; and after death toxin may be recovered from the nerves as readily as from the internal organs. The peripheral portions of the nerves are found to give up more toxin than those portions nearer the spinal cord. In other words, *the nearer the toxin gets to the spinal cord the more impregnably entrenched does it become in the nerve tissue*. A much larger amount of toxin must be injected into the periphery of the limbs (*e. g.*, subcutaneously in the toes) to cause death, than in the central portions of the limbs (*e. g.*, intramuscularly); in other words, *the readier the access of the toxin to the central nervous system the less is the amount required to kill*. The minimal lethal dose is much less if injected into a nerve than if injected anywhere else; it is less when injected intramuscularly than if injected subcutaneously or intravenously.

The *incubation period* depends on the distance from the cord of the site of injection of the toxin. If the toxin is injected into one of the lower extremities of a rabbit, the first definite symptoms appear about the third day; if the injection is made into the subdural space of the cord, or into the cord itself, the incubation period is only a few hours. Division or resection of nerves after intramuscular injection of toxin could save the lives of rabbits only if done within about one hour of the time of injection of the toxin; but even in fatal cases life was

² In animals rapid emaciation sometimes has followed administration of tetanus toxin, when no tetanic symptoms were produced. Probably these cases, which are described as *tetanus sine tetano*, are due to the action of the toxin on structures other than the nervous system.

prolonged more than when the nerves were not cut, no matter if an interval of from eighteen to forty hours elapsed between the injection of the toxin and section of the nerves of the limb (Sawamura). The use of cocaine in the afferent nerves, or the division of all sensory nerves (leaving the motor nerves intact) may retard the development and diminish the severity of the course of tetanus, but it cannot prevent it. The same is true of intradural division of the posterior nerve roots (Sawamura). If local tetanus has not lasted long, it can be stopped by section of the nerves or by use of curare; but if it has lasted over two days, the tetanic muscle cramp will not be influenced by these methods and will persist even after death. According to Gumprecht this is to be explained as a fatigue phenomenon, commonly seen in physiological experiments; he never found reactions of degeneration present.

By what structures of the nerve does the toxin reach the cord?

Gumprecht (1894) and Stintzing (1898) claimed that it went only through the peri- and endoneurium, passing thence mostly into the cerebrospinal fluid, but also entering directly into the spinal cord, though in smaller amounts. In support of this theory, Gumprecht found that if he injected toxin into the subdural space of the cord in the lumbar region, local tetanus began first in the animal's hind legs. Stintzing found that the cerebrospinal fluid of two men, very ill with tetanus, was very toxic for mice, while the blood of these patients was not toxic. But Meyer and Ransom (1903) repeated Gumprecht's experiment, and found, if care was taken not to wound the pia or the cord, that general (descending) tetanus was produced before local (ascending) tetanus; moreover, they did not find the cerebrospinal fluid toxic either in patients or experimental animals. These latter investigators (l. c., Obs. 32, S. 413) injected a moderate amount of toxin into the sciatic nerve of a highly immunized rabbit, and nevertheless fatal ascending tetanus developed; yet examination showed that the blood, the cerebrospinal fluid, and the nerve lymph contained active antitoxin. The amount of antitoxin in the nerve lymph, however, was very small—very much less than that in the blood. A twenty-five-fold lethal dose of toxin had been without effect when injected subcutaneously, because at once neutralized by the antitoxin in the circulating blood; two drops of the blood contained more than enough antitoxin to neutralize the fatal dose of toxin injected into the nerve. Their conclusion was that the toxin when injected into the nerve must have reached the cord by way of the axis cylinders, since the antitoxin in the nerve lymph could not neutralize it; but it seems to us an equally correct conclusion that the amount of antitoxin in the nerve lymph was insufficient, even if that in the blood was superabundant. Further reference to this question is made in connection with the prophylactic use of antitoxin (p. 817).

All that it seems safe to conclude is:

1. The toxin surely ascends the nerves by way of the axile cylinders (perhaps by means of a centripetal protoplasmic current), and in this way can produce a severe tetanus ascendens.

2. The transmission of toxin through the peri- and endoneurium cannot be excluded, and the toxin absorbed in this way may play an important part in the development of local tetanus.

The above facts, briefly outlined, are those which prove that the toxin ascends the peripheral nerves to the cord.

2. *The toxin spreads to neighboring parts of the spinal cord.* The diffusion of the toxin in the spinal cord has been demonstrated in several ways. Marie and Morax injected toxin into the lumbar swelling of the cord, and thereafter found toxin in the dorsal cord. If the cord is cut through above the lumbar swelling, tetanus develops only in the lower extremities in cases where toxin has been injected previously into the sciatic nerves, and no tetanus develops in the parts supplied by the cord above the point of section. Moreover, the usual sequence of symptoms in ascending tetanus bears witness to the gradual spread of the toxin within the spinal cord—first the wounded extremity becomes tetanic, then the other lower limb; next the back and abdomen, then the fore limbs, and finally, the neck and head.

Invasion of the sensory portions of the cord also occurs, and is responsible for the extreme hyperexcitability, evidenced by the facility which very feeble peripheral stimuli possess of causing severe clonic convulsions during the disease. If the toxin is injected experimentally into the sensory nerves it is blocked effectually by the ganglia on the posterior roots; if injected into the posterior roots on the proximal side of the ganglia, a very painful form of the disease, termed Tetanus Dolorosus, is produced; and the animals die of exhaustion before the motor phenomena, so characteristic of the disease in its ordinary forms, have had time to develop.

3. *Some of the toxin enters the general circulation.* This is proved primarily by the fact that toxin has been found in the blood on numerous occasions, in experimental animals and in man. It was first found in the blood of man by Nissen in 1891.³ *This toxin eventually reaches the cord and produces descending tetanus.* This is proved, because even after all the nerves of a limb have been cut, tetanus descendens can be produced by injecting toxin into the enervated extremity, though many times the usual lethal dose is required. It is certain that the toxin reaches the cord from the general circulation chiefly, if not only, by being brought into contact first with the end-plates of the various motor nerves, and by

³ According to Stintzing, however, it could not be demonstrated in the blood by Rosenbach, Schulz, Billroth, Moritz, Henoch, and Engelmann.

being transferred through these nerves to the cord. This occurs even when the toxin is injected intravenously, but at present it cannot be certainly proved that no toxin reaches the central nervous system *directly* by the blood; but it seems highly improbable.

MORBID ANATOMY OF TETANUS. Thus far it has not been possible to find, in the peripheral or central nervous system, or elsewhere, any changes which are specific for tetanus. There may be swelling and fragmentation of the axis cylinders, and hemorrhages with vacuolation of the cells in the anterior horns of the spinal cord; but these changes cannot be distinguished from those due to other causes. The recovery of the *Bacillus tetani* from the point of inoculation often is impossible, and scientific confirmation of the diagnosis must rest in many cases upon the reproduction of tetanic symptoms in animals by the injection of toxin extracted from the patient. In the vast majority of cases the clinical diagnosis is quite certain enough without any confirmatory evidence from the laboratory.

Of 15 cases studied bacteriologically, Huber reports that the *Bacillus tetani* was recovered from the wound in 8. This seems a larger proportion of successful cultures than in most series of cases. In our own series of 23 cases, search was made only in a few instances, but never was successful.

In 2 patients, in whom the wound was in the lower extremity, Porter and Richardson excised the inguinal lymph-nodes, and in both cases found tetanus bacilli in the nodes.⁴ This demonstrates that the bacillus does not, in all cases, remain in the immediate vicinity of the point of entrance, and suggests that the persistence of symptoms of toxin absorption even after wide excision or amputation of the primary focus may be due to toxin elaborated by bacilli lodged in the anatomically related lymphatics.

CAUSE OF THE SYMPTOMS OF TETANUS. The toxin stimulates the motor cells of the spinal cord, with the result that the muscles controlled by these cells are thrown into tonic spasm; the toxin, as already noted, also renders the sensory side of the cord extremely susceptible to external stimulus, so that very insignificant stimuli, such as the slamming of a door, jarring the patient's bed, a sudden draught of air, etc., will bring on clonic convulsions, or at least will greatly intensify, for the moment, the tonic spasms.

THERAPEUTIC INDICATIONS. These may be summarized as follows:

1. To prevent the development of tetanus.
2. To remove the source which supplies the toxin, *i. e.*, the bacilli of tetanus.
3. To head off and neutralize the toxin already formed.

⁴ Schnitzler had found the bacilli in the inguinal lymphatics at autopsy, and Fricker also had found them in the related lymph-nodes.

4. To depress the functions of the spinal cord.
5. To sustain the life of the patient by proper nourishment, nursing, etc.

PROPHYLAXIS OF TETANUS.

It is well known that *certain classes of wounds*, received in certain surroundings, are more often followed by the development of tetanus than are ordinary wounds. The *Bacillus tetani* is anaërobic, and is found especially in garden soil, barn-yards, stables, etc. Probably it normally infests the intestinal tract of horses and cattle, and is deposited with their dung. So long as the mucosa of their gastro-intestinal tract is intact, they are not liable to infection by this channel, on account of the antitoxic properties of the intestinal juices, especially the bile (H. Vincent). Matas suggests that postoperative tetanus may be due to tetanus bacilli, latent in the patient's intestinal tract, ingested with uncooked food, and infecting the operative wound by fecal contact. There is no good evidence that it is due to the use of infected catgut. According to Fox, tetanus bacilli are found in the feces of 5 per cent. of mankind; and in the feces of 20 per cent. of men who work about horses.

On these accounts, wounds received by farmers, gardeners, stablemen, etc., are especially liable to be infected with tetanus bacilli. Wounds by farming or gardening implements; wounds by axes, as in felling trees; machinery crushes; wounds produced by dragging in the dust, by kicks or bites of horses; wounds by nails, spikes, etc., incrustated with dirt and rust—these are the causes most to be feared.

In our own series of 23 cases, there were 10 in which the wound was contaminated by country earth or street dust; 2 caused by splinters from the floor; 5 by rusty nails or iron spikes; 3 due to machinery accidents; and 1 each to a gunshot wound, puerperal infection, and an explosion.

Inoculation is favored by *anaërobic conditions of the wound*. Especially favorable sites are wounds in which the tissues are sloughing; the best culture medium for tetanus bacilli, according to Tarrozzi, is that which contains some dead organic tissue. Thus punctured wounds, contused and lacerated wounds, and wounds in which there are foreign bodies (earth, machine oil, splinters, wadding, etc.), offer favorable conditions for the development of any bacilli present. A mixed infection, especially with saprophytic bacteria, is favorable because these organisms, being aërobic, absorb all available oxygen and provide anaërobic conditions for the tetanus bacilli.

Care of the wound is naturally the first step in the prophylaxis of tetanus. Such wounds as are considered to offer favorable soil for the development of tetanus bacilli should be treated with even

more than ordinary antiseptic precautions. If the original wound is properly treated, the development of tetanus is unusual. Of our own 23 patients, only 7 had received proper treatment of the wound; and, even in these 7, extra precautions not adopted no doubt would have been taken if the possibility of the development of tetanus had been kept in mind. It is our firm belief that efficient care of the wound as soon as possible after it is received is by all means the most important feature in prophylaxis. We have never yet had a case of tetanus develop in a patient whose wound has been under our care from the first.

Here we must call attention to Case 11 of the present series. This patient was seen by both of us in the Out-patient Department a few hours after his injury was received. Recognizing the gravity of the wound, we referred him at once to the ward of the hospital. Unfortunately he was permitted to return home almost immediately, without proper treatment of the wound, and ten days later developed acute tetanus, from which he died. Efficient treatment of the wound at first might have altogether prevented tetanus, or at all events might have lessened its severity.

Our method of treating a suspected wound is as follows: (1) The surrounding skin is painted with a 3 per cent. alcoholic solution of iodine. (2) Then *all parts of the wound are made accessible*, by wide incision if necessary. (If a punctured wound of the foot, of suspected nature, exists, it is freely opened to its depths, dividing the plantar fascia as far as necessary. If the patient lives far from the hospital, and cannot return home on crutches, he is kept in the ward.) (3) The wound is mechanically cleansed by scissors and forceps, and then is thoroughly swabbed out with the iodine solution. (4) The wound is lightly filled with gauze soaked in the iodine solution, and is properly dressed. We *avoid all caustics*, as they kill the tissues, and the resulting sloughs, even if minute, furnish favorable sites for the growth of tetanus bacilli. At subsequent dressings (daily at first) the wound is exposed by removal of the iodine gauze, is irrigated with peroxide of hydrogen until active effervescence ceases, and is again filled with gauze soaked in the iodine solution. This method of dressing is continued until healthy granulations are formed. Bockenheimer has concluded from experimental work that the best dressing for these wounds is Balsam of Peru which he believes is antibacterial to the tetanus bacilli. Hessert commends this dressing.

*The Prophylactic Use of Antitoxin.*⁵ This was first extensively employed in veterinary practice by Nocard, in 1895, and is found

⁵ For the following information we are indebted to Dr. A. Parker Hitchens, of Glenolden, Pa.: The United States Government has established a standard method for testing the strength of tetanus antitoxin: "The immunity unit for measuring the strength of tetanus antitoxin shall be ten times the least quantity of antitetanic serum necessary to save the life of a 350-gram guinea-pig for ninety-six hours against the official test dose of the standard toxin furnished by the Hygienic Laboratory of the Public Health and Marine Hospital Service." The official

to be almost of absolute value. That it is not by any means always effective when used in man, is only too well known. The reasons for the difference in its action in horses and in man must depend, as pointed out by Solieri, on one of two factors: either it is not so useful or it has not been properly administered. (1) Perhaps the fact that horses (in which its use is most successful) are treated by antitoxin derived from their own serum, while human patients are treated by an alien serum (horse), makes the difference. But to this supposition (and it is little more) it may be replied that other animals, such as cattle and sheep, are well protected by the horse serum. (2) The most reasonable explanation of the numerous failures of antitoxin to prevent the development of tetanus in man lies in the faulty manner in which it has been administered, in most cases. Remertz has tabulated 55 cases where tetanus developed in spite of the prophylactic use of antitoxin; in 38 of these cases the diagnosis is positive; and as only 30 of these patients died (53 per cent.) it is evident that the antitoxin at least rendered the disease less fatal; but even with all allowances the mortality in these cases cannot be brought below 40 per cent.

There are three things to be considered in the matter of the prophylactic use of antitoxin: (1) The frequency with which it should be given. (2) The site of the injection. (3) The quantity to be administered.

1. *The frequency of prophylactic injections.* It appears to be a well-ascertained fact that the antitoxin is all eliminated from the system in about eight or ten days after the injection. It remains in practically undiminished amount for a week, and then rapidly diminishes to nothing in the course of two days (Dehne and Hamburger). As the tetanus bacilli, if any are lodged in the wound, may not begin to produce any toxin until at least as long a time

test dose of toxin is one hundred times the smallest quantity of toxin which will kill a guinea-pig within ninety-six hours. Dr. Hitchens adds that Rosenau and Anderson (1908) found in a German serum which they examined 330 units per c.c., and in some French serums from 40 to 66 units per c.c. Dr. Hitchens examined some French serums in 1910, and found they contained from 30 to 50 units per c.c. He permits us to publish the following results of other examinations made by him in 1910. He thinks that the tests may have been a little too rigid, and that the results noted below are about 15 per cent. too low.

Behring (5 fach.)	220 units per c.c.
Behring (5 fach.)	200 units per c.c.
Berne	12 units per c.c.
Höchst (4 fach.)	110 units per c.c.
Höchst (5 fach.)	250 units per c.c.
Krakau—less than	1 unit per c.c.
Vienna	120 units per c.c.
Lister Institute (veterinary)	30 units per c.c.
Rebman, London, less than	1 unit per c.c.

If the serum at present in use in these countries remains as weak as in these samples, it is evident that the doses of antitoxin administered abroad for therapeutic effect have been quite insufficient. In this country tetanus antitoxin is supplied in tubes each of which holds 10 c.c., the strength being 1500, 3000, or 5000 units per 10 c.c. according to the concentration.

as this has elapsed, it is manifestly important, if the antitoxin is to be of use, that some should be present in the system for two or three weeks after the receipt of the injury. In many cases the tetanus bacilli do not enter the wound at the time of the accident, but are introduced secondarily by the carelessness of the patient in neglecting to return for dressings, and in attempting to care for the wound in septic surroundings at home; in such cases surgery can scarcely be held responsible. But even if present in the wound from the first, the bacilli may lie dormant for weeks in spore form, before development occurs with the production of toxin.

Vaillard cites 6 cases in which the period of incubation was over a month, in 1 of which (Terrier) it was eighty-seven days. In Case 4 of our series, with an incubation period presumably of eight weeks, the onset was very gradual, but the disease then developed in frightfully acute form and was rapidly fatal. Fox says that tetanus spores injected into a guinea-pig have remained latent for four months, and have then, without apparent cause, produced an outbreak of the disease. In some such manner as this, no doubt, are to be explained the not very unusual cases where the symptoms of tetanus recur some time after apparently complete recovery from a frank attack of the disease. Fink reports two severe relapses at intervals of several months, due to the development of latent spores; Fedden records such a case, where symptoms recurred over one month after complete recovery; and Reynier narrates a rather mysterious case where slight recurrent attacks of tetanus occurred throughout a period of six years, and in which finally a typical and very severe attack occurred, apparently caused by the hypodermic injection of a quinine salt.⁶

The necessity for a second injection of antitoxin about the eighth or tenth day is thus very evident, and it may be well to administer a third injection during the third week. Solieri insists that this injection must be renewed every eight or ten days until all necrotic tissues are removed and there is a clean granulating surface. In almost all of the 55 cases, noted above, in which tetanus has developed in spite of the prophylactic use of antitoxin, *the injection was not repeated*.

But that even repeated injections may prove ineffectual is demonstrated by the well-known case recorded by Maunoury: 10 c.c. of antitoxin was injected at once after the injury; this was repeated in six days; and again six days later a third injection was given. Twelve days after the third injection, as the patient complained of severe pain in the wounded part, a fourth injection was given, and the limb was amputated. In spite of this, three days later (twenty-seven days after injury) tetanus developed,

⁶ Subcutaneous or intramuscular injections of quinine salts may arouse latent tetanus spores, because they cause local necrosis (Vincent, 1904). This subject is well discussed editorially in the Indian Medical Gazette (1911, xlv, 141 to 142). This teaching is controverted by Palmer and by McCampbell; the latter holds that quinine can be held responsible only if there is already present a secondary (pyrogenic) infection.

and the patient died of severe tetanus in twenty-four hours. (Was this possibly a case in which some bacilli had lodged in the lymph nodes, or was it that the antitoxin injected at the end of the second period of six days had all escaped from the body at the end of the next twelve days, when the fourth injection was given?).

2. *The site of the injection.* In most of the reported cases no details of the site of injection are given, but in such cases it is presumed that the antitoxin was administered subcutaneously.

Calmette, and later McFarland, applied antitoxin in powdered form directly to the wound, in experimental prophylaxis, and found it of great value. Lop, however, found it did not prevent the development, eight days after injury, of tetanus fatal in three days, though the wound was powdered with antitoxin one-half hour after the injury, and again three days later. Luckett had a similar experience. It may be, as suggested by Tuffier, in the discussion of Lop's case, that the antitoxin was absorbed by the dressings applied instead of by the wound. Remertz refers to two other cases in which the use of powdered antitoxin proved ineffectual.

The subcutaneous use of antitoxin in prophylaxis is open to the same objections raised against this method of therapeutic administration (*q. v.*). In any circumstances the antitoxin should be given as near to the wound as possible, so as to flood the tissues in the immediate vicinity; and the injection should be deep, intramuscular if possible, so as to permit its rapid absorption by the motor nerves. If the antitoxin can reach the peripheral nerves before any toxin that is formed reaches them, the likelihood that the toxin ever will reach the spinal cord is much decreased. If any nerves are exposed in the wound the antitoxin should be injected into them.

This was the idea of Meyer and Ransom, who thought the imperilled spinal-cord centres might be protected from the toxin by blocking the afferent nerves with antitoxin. They proved that if one sciatic nerve of a rabbit was injected with antitoxin, and simultaneously both legs below the knees were injected with toxin, then only the protected limb remained free from tetanus or developed it very late. Sawamura repeated these experiments: first he injected twice the lethal dose of toxin in the leg, and from sixty to ninety minutes later injected antitoxin into the sciatic nerve of the same limb; 6 out of 8 rabbits thus treated did not die, and the limb so treated remained free from local tetanus in all, even in the 2 fatal cases where death was caused by general tetanus. The 6 control animals (not protected by antitoxin in the nerve) all developed local tetanus, and 2 died of general tetanus.⁷

⁷ The fact that intraneural injections of antitoxin block the further progress of toxin along the nerves, is good evidence, it seems to us, either that the toxin ascends in large amounts through the lymph channels of the nerves, or that antitoxin can be readily absorbed by axis cylinders which are in its neighborhood. It evidently is not necessary for the injecting needle to penetrate each and every axis cylinder of the nerve trunk.

If antitoxin was injected subcutaneously or intravenously, even in two or three times the quantity, it was powerless to prevent the development of local tetanus. The experiments conducted by v. Graff, to test the prophylactic value of antitoxin administered intravenously, are detailed below.

3. *The quantity of the injection.* Usually 1500 units is the amount employed as a prophylactic dose. Remertz thinks that even if the injection is made very soon after the injury, the least amount that can be useful as a prophylactic dose is from 2 c.c. to 5 c.c. (= 20 A. E.); according to Hitchens' table (p. 815) this is equivalent to about 1500 units, U. S. A. Remertz says that Lotheisen thought 100 A. E. was the proper prophylactic dose. Taking the average weight of persons injected as 150 pounds, and figuring out the potency of the antitoxin from the known value of a unit (U. S. A.), we find that 1500 units is a little over two thousand times the amount necessary to neutralize the minimal lethal dose of toxin in such an individual. Such an amount is by no means excessive, in view of the fact that the amount of antitoxin required to prevent death increases in geometrical progression with the lapse of time. After the lapse of one hour, twenty-four times as much antitoxin is required as when antitoxin and toxin are injected simultaneously (Remertz). Certainly antitoxin will be more useful if injected in the immediate neighborhood of the wound than elsewhere, as it will then be in more concentrated form as it comes into relation with the forming toxins.

Objections to the prophylactic use of antitoxin. The chief objection is the expense. Unpleasant symptoms from its use are scarcely known, even when it has been used in massive doses as a therapeutic measure. The site of the injection often is painful, and if carelessly given, harm may result.

We are cognizant of one case where the injection was made by a trained nurse, by order of a physician. The needle was introduced on the outer side of the thigh, but too near the knee; the result was that the antitoxin was injected into the subfemoral bursa, and the patient was laid up in bed for several days, with "water on the knee."

Occasionally, in susceptible individuals, an erythematous or urticarial rash develops and multiple arthritis has been reported (Reynier), but other evidences of anaphylaxis do not appear to have been observed.⁸

In conclusion, it may be said that the worst reproach that can be made against the prophylactic use of antitoxin is that, while it is harmless when carefully administered, it may be useless. That it never is useful has not been proved; and we believe that so long

⁸ Riche has recorded a death following the prophylactic injection of tetanus antitoxin in a patient under the care of Rilhac; but the cause of death was undetermined.

as a possibility of its usefulness exists, it is proper to employ it in the case of suspected wounds. In none of the patients in our series had a prophylactic injection been given. At least 1500 units should be given, in the immediate neighborhood of the wound; it should be injected deeply into the muscles; or if possible, into the nerves (when a smaller quantity will suffice). This injection *should be repeated* at the end of seven or eight days; and, if possible, a third injection should be given during the third week.

Finally, a few words may be said about "*Fourth of July Tetanus.*" In spite of diligent, and we believe unprejudiced, study of the subject, we have been unable to convince ourselves that such injuries received on "the day we celebrate" are more liable to be followed by tetanus than other contused or lacerated wounds.

During the years one of us was on duty at the Children's Hospital, Philadelphia, where many such cases were treated every year, antitoxin never was employed as a prophylactic (the hospital being unable to afford it), but the wounds were cleansed as above described with most meticulous exactitude; yet not one case of tetanus due to such an injury ever occurred. Indeed, we have never seen anywhere a case of tetanus due to such an injury.

We believe, however, that the campaign for the use of antitoxin as a prophylactic has accomplished a marked reduction in the incidence of tetanus; but we hold that this result may be attributed as rationally to better care of the wound as to the antitoxin employed, because a physician who thinks of antitoxin thinks also of tetanus, and the thought of possible tetanus impels him to take proper care of the wound. Moreover, in only an extremely small proportion of cases has the injection been repeated.

(To be continued.)

THE OCCURRENCE OF CANCEROUS CHANGES IN BENIGN NEWGROWTHS OF THE SKIN.

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IN many instances the line which separates malignant from non-malignant cutaneous tumors is a shadowy one. Heidingsfeld,¹ in a comparative histologic study of 5 cases of "benign cystic epithelioma" (one of which, judging from the slides exhibited, was an example of syringocystadenoma), and one each of morphea-like epithelioma and carcinoma epitheliale cicatrisans, has expressed the opinion that all growths of the Brooke² type are premalignant

¹ Jour. Amer. Med. Assoc., lix, 256.

² British Jour. Dermat., 1892, p. 269.

in character and structure. While few pathologists will agree with Heidingsfeld in this assertion, the fact remains that in a few instances, as in the cases of multiple benign cystic epithelioma reported by J. C. White,³ Jarisch,⁴ Stelwagon,⁵ and Dennie and myself⁶ there has been a concomitant epitheliomatosis of the rodent ulcer type.

McDonough⁷ has recently made an interesting and valuable contribution to the pathology of the skin from the eyelids and the nasofacial grooves. He takes the view that the majority of tumors affecting the orbitofacial and nasofacial grooves are of epithelial origin, and atavistic of both the lower eyebrows and the specialized glands found in these regions in many of the mammalia, and believes that all of the growths, from a simple lanugo hair follicle to a rodent ulcer, are links in one chain, the former being the head or most mature, the latter the tail or most embryonic. As they are all links, the histologic differences of any one clinical entity are at once apparent. This explanation is exceedingly plausible, particularly as regards the relative frequency of growths in this region; but unfortunately it does not go far enough. While tumors of the various types included (adenoma sebaceum, acanthoma, or epithelioma, adenoides cysticum and its subvariety, tricho-epithelioma of Jarisch, "syringoma," and rodent ulcer) are often found in the areas indicated, in the majority of instances their distribution is much wider, and, in several of the cases reported, the eyelids and nasofacial grooves were not involved at all.

Adamson,⁸ in discussing 2 cases of multiple rodent ulcer, gives an admirable and concise review of the subject in general, and discusses the possible interrelationship of rodent ulcer, multiple rodent ulcer, and acanthoma adenoides cysticum with and without accompanying manifestations of malignancy. He points out the features possessed by all of the growths in common—derivation from the basal layer of the epidermis or from the hair follicle, occurrence of the growth in the form of cell masses having a palisade marginal layer and a centre of rounded or oval cells, the tendency to cyst formation, and the presence of a newly formed capsule of connective tissue surrounding the epithelial masses. For contrast, he emphasizes the highly vascular character of the fibrous elements in the lesions of rodent ulcer, together with the plasma-cell exudate at the advancing margin of the growth, and the ever-present tendency of the outlying groups of epithelial cells to invade the tissues beyond the main body of the tumor.

³ Jour. Cutan. Dis., 1894, p. 477.

⁴ Arch. f. Dermat. u. Syph., 1894, p. 164.

⁵ Diseases of the Skin, Philadelphia, 1910, p. 634.

⁶ Jour. Amer. Med. Assoc., lviii, 333.

⁷ British Jour. Dermat., 1912, p. 291.

⁸ Lancet, London, clxxv, 1133.

As Adamson succinctly states, "histologically the lesions of rodent ulcer have many features in common with those of epithelioma (acanthoma) adenoides cysticum, and they are probably derived from the same part of the epidermis. Pathologically they differ in that the one tends slowly to invade and to destroy the surrounding tissue, while the other has no such tendency."

For several months I have had under observation two unusual cases of rodent ulcer, the histories of which are of interest in relation to this subject.



FIG. 1.—Case I. Acanthoma adenoides cysticum, showing size and distribution of tumors.

CASE I.—A. G., female; married; housewife; aged fifty-one years. This patient has been under the care of my friend, Dr. Oliver H. McCandless, a Röntgenologist of Kansas City for the past four or five years, and it is with his permission that the history is here given.

Family History: So far as the patient is able to discover, only one other member of the family, a daughter, has ever had a similar cutaneous disorder.

Personal History: The patient is a native of Indiana, and a resident of Rosedale, Kansas. Her health has always been good. She has never had a skin disease other than the one from which relief is now sought.

Present Illness: When the patient was about fifteen years of age, several small discrete papular growths appeared on her face and back. The lesions were thought to be warts, and little attention was paid to them. In course of time the tumors increased in

number, until in 1906 there were more than seventy of the lesions, varying in size from a millet-seed to an English walnut, asym-



FIG. 2.—Case I. Rodent ulcer of inner angle of left eye. Acanthoma adenoides cysticum on face and forehead.

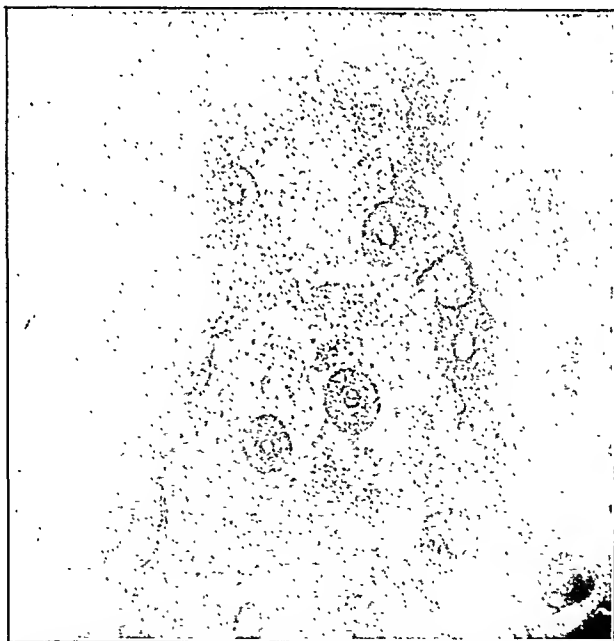


FIG. 3.—Showing histologic features of a typical tumor in acanthoma adenoides cysticum.

metrically distributed over the face, neck, and chest. The majority of the tumors were mushroom-shaped, with a short pedicle and a shiny, button-like top. In 1907 one of the growths was excised and examined microscopically by Dr. Frank J. Hall. It was found to be a typical *acanthoma adenoides cysticum* of Brooke.

Prior to the case coming under the care of Dr. McCandless some of the lesions had been curetted, cauterized with acids, or treated with an electric needle. Since the patient has been in his charge, dependence has been placed for the most part on the x-rays. About one year ago a small cystic tumor appeared at the inner canthus of the left eye, at a point where, so far as known, no lesion had previously existed. In the course of a few weeks this tumor broke down and an ulcer developed, clinically indistinguishable from an epithelioma. Despite treatment this ulcer has continued to increase in size.

Examination: The patient is a well-preserved woman, with brown hair and eyes. Irregularly scattered over the face, neck, and trunk are sixty or more solid tuberous growths, varying in size from a pin-head to an ordinary checker. Many of the lesions are tender on pressure, although only a few show evidence of the presence of inflammation. Several scars, the sites of lesions that have been removed, are to be seen on the forehead and chin. At the inner angle of the left eye, and extending downward to the ala of the nose, is a superficial ulcer, triangular in outline, with rounded, shiny, indurated borders. Permission to perform a biopsy was refused. Although some of the nodular lesions showed inflammatory or ulcerative changes it is probable that these were coincident with healing, and were the result of treatment.

CASE II.—L. T.; female; married; housewife; aged twenty-three years. This patient was first admitted to Professor Walter S. Sutton's service (surgical) at the University Dispensary, and later was referred by him to the dermatologic department for observation and treatment.

Family History: This patient is the daughter of the woman whose case history has just been given. She also has a daughter, three years of age, but the child's skin is free from lesions of any kind.

Personal History: The patient is a native and a resident of Wyandotte County, Kansas. Her general health has always been excellent.

Present Illness: In August, 1905, the patient first noticed the presence of several small, flat-topped "moles" on her forehead, face, and neck. The little tumors were pink in color, painless on pressure, and irregularly distributed over the affected areas. Since that time a new papule has occasionally appeared, the older ones, with a single exception, having ceased to increase in size after they had attained the diameter of a grain of wheat. In

the exception noted the lesion, which was located on the right side of the neck, near the hair margin, broke down, in January, 1911, and the resulting ulcer gradually increased in area until it was a centimeter or more in diameter. The margin was elevated, nodular, and pearly, and, when the growth was excised, by Dr. Walter Sutton, in December, 1911, it was found to be a typical rodent ulcer.



FIG. 4.—Case II.—Multiple rodent ulcers, showing size and distribution of lesions.

Examination: The patient is a brunette, with brown hair and eyes. On parts other than the face and neck her skin is smooth and unmarked. The texture of the skin of the face is somewhat coarse, and there are present, even in the winter time, large numbers of freckles. The integument is soft and pliable, however, and there is no suggestion of xeroderma. Scattered irregularly over the forehead, face, and neck are a number, fifty-two in all, of small, flat, or round-topped, somewhat burnished, flesh colored papules, varying in size from a millet-seed to a large grain of wheat. The little nodules are firm to the touch, and painless on pressure. None are broken down or ulcerated. Three of the lesions were

excised by means of a small cutaneous punch, under cocaine anesthesia, and examined microscopically. All three were similar in structure, typical epitheliomas of the rodent ulcer type, the proliferating elements being derived from the basal layer of the epidermis.



FIG. 5.—Case II.—Showing histologic features of a characteristic lesion.

TREATMENT. Practically all of the remaining tumors have been removed by means of Pusey's carbon dioxide snow. The method is almost painless, and proved exceedingly efficacious, only a small depressed scar remaining to mark the site of each former growth. The comparatively slight amount of irritation resulting from the application of this agent renders it far preferable to the needle or to chemical caustics or the eurette in cases of this character. More than a year has elapsed since the first growths were removed, and no untoward symptom of any kind has developed.

While it is hardly probably that the presence of acanthoma adenoides cysticum in the first case here reported had any direct bearing upon the subsequent appearance of the rodent ulcer, the fact that the patient's daughter developed tumors of a malignant type is exceedingly suggestive of a more than casual connection between the two conditions. Judging from a fairly exhaustive study of three different cases of acanthoma adenoides cysticum, I believe the lesions to be embryonic in origin, and similar, in some respects, to those of syringoecystadenoma. The evenness and

regularity with which the epidermal processes extend into the adjacent connective tissue, the retention of many of the characteristic contour and tinctorial qualities of the epithelial elements, the freedom from associated plasma-cell infiltration, and in the vast majority of instances the total absence of malignant tendencies of any kind all point to the correctness of this hypothesis.

On the other hand, in rodent ulcer and allied types of epitheliomas one of the most distinctive and striking features is the apparent freedom of the growth from guidance or restraint of any kind, and the manifest insatiable desire of the constituent cells to tear down and destroy normal structures with which they come in contact.

Although the parasitic nature of malignant growths in man is as yet unproved, the result of the investigations of Erwin F. Smith⁹ and others on a strikingly similar disease in plants ("crown gall," due to the bacterium *tumefaciens*) is encouraging, and it is probable that the discovery and isolation of the causative organism, or organisms, is only a matter of time. Certain states and conditions of the skin undoubtedly predispose to attacks of this kind, and a suitable soil may be inherited as well as acquired. That the changes occasioned by the presence of such an affection as *acanthoma adenoides cysticum* renders the skin more susceptible to cancerous involvement, however, I consider improbable, and unproved by the evidence now at our disposal.

THE USE OF ANTITYPHOID VACCINE DURING THE COURSE OF AN EPIDEMIC.¹

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PREVIOUS REPORTS. The use of antityphoid vaccine in military and civil life, particularly in institutions, has been carefully studied. The statistics which have been compiled have presented most prominently the types of local and general reactions observed, the strains of microorganisms used, and, to a much less extent, studies upon agglutinins, bacteriolysins, phagocytosis, and some rather insufficient references to the "negative phase."

However, records of its use as a prophylactic agent during the course of epidemics have been meagre. The earliest record is that by Cullinan, of Dublin (quoted by Wright²), who reports inoculations of over 500 persons during an epidemic lasting five months

⁹ Moore, *Jour. Cutan. Dis.*, 1912, p. 515.

¹ Read in the Section on Medicine of the College of Physicians of Philadelphia, April 28, 1913.

² *British Med. Jour.*, October 26, 1901, p. 1226.

in the Richmond Asylum. Among those inoculated only 1.35 per cent. contracted the disease, all of whom were in the incubation stage of the disease at the time; 14.9 per cent. of 114 uninoculated nurses subsequently developed typhoid fever. Leishman,³ Wright, and Semple inoculated 100 attendants in the Barming Asylum during the Maidstone epidemic in 1897; none of those vaccinated developed the disease.

It was used extensively in an epidemic in Torrington,⁴ Connecticut, during the summer of 1911, only one case occurring among those vaccinated. Russell⁵ mentions its use during an epidemic in Cuba in which 2500 marines were subject to exposure, and again in Cedar Rapids, Iowa, during 1912. Ravenel⁶ refers to its use during an epidemic in a small Wisconsin town during the same year. Vincent⁷ reported the results obtained by him in Algiers and Morocco. However, as was subsequently pointed out by Metchnikoff,⁸ the disease was endemic and not epidemic in the countries in which Vincent's studies were made.

Spooner⁹ reports the results of his observations in a small community in Vermont, in which 65 persons were exposed. 29 of these were inoculated after 17 cases of typhoid fever had been reported; 19 persons refused vaccination; 5 (26.3 per cent.) of the latter developed the disease, while only 1 (3.5 per cent.) of the 29 inoculated persons became ill.

In these reports, it should be observed, the origin of the infection, the means of transmission, the time of disinfecting the transmitting agent, and the relation of the use of vaccine to the period of pollution and use of the transmitting agent have not been noted.

It is the purpose of this paper to contribute to the literature, studies on the use of vaccine during the course of an epidemic in Troy, Bradford County, Pennsylvania. The writer was assigned in charge on October 12, 1912, by Dr. Samuel G. Dixon, Commissioner of Health, by whose permission the results are presented.

TROY EPIDEMIC. A brief history of the essential features must be given, although the full report¹⁰ has been published elsewhere.

The Troy epidemic was entirely water-borne. It was designed that the water should be obtained from a combination of spring and ground-water supply, but there is reason to believe that it always included the waters of a stream which traversed the points of collection. The deposition of sewage near the stream occurred some time during the month of August or early in September, and was traced directly to a typhoid carrier; the latter, a male,

³ Jour. Roy. Inst. Public Health, London, 1910, vol. xviii.

⁴ Russell, Jour. Amer. Med. Assoc., October, 1912, p. 1368.

⁵ Loc. cit.

⁷ Bull. de l'Acad. de Méd., Paris, December, 1911.

⁸ Acad. des. Sci., Paris, June, 1912.

⁹ Jour. Amer. Med. Assoc., October, 1912, p. 1359.

¹⁰ Hunt, Jour. Infec. Dis., Chicago, May, 1913.

⁶ Ibid.

aged twenty-four years, had suffered with the disease, from which he had fully recovered, seven months prior to the epidemic. The examination of his feces and urine was negative on the first attempt; on the second examination, made some six weeks after the onset of the epidemic, eight to ten colonies of the *Bacillus typhosus* were recovered from each cubic centimeter of the diluted feces; these were properly identified, and were subsequently used to study the agglutination of the sera from patients in Troy.

After an unusual period of drought there were two successive and unusual rainfalls, the first one occurring on September 15 and the second during a period of three days, from September 22 to 25 inclusive.

The onsets of the cases occurred at the maximum between eleven and fourteen days after each rainfall. The two curves produced (as determined by dates of onsets) show the fastigia occurring on September 28 and on October 8 to 11. The water was probably continuously polluted from September 15 to October 14, with two periods of maximum pollution occurring immediately subsequent to the rainfalls mentioned. During this period there was a gradual subsidence of the flood waters, so that at the time of disinfection on October 14 the stream was practically at its normal flow. However, there was normally no period of subsidence of the waters used for the municipal supply because the reservoirs were insufficient for storage purposes. These factors are of importance as aiding in the continuance of the infecting agent, and would indicate that while some dilution of the sewage undoubtedly occurred, there was a continuing pollution to which the users of the water were exposed up to the date of disinfection of the supply and of the distributing system. A careful study of all conditions indicates that the incubation periods of the last persons to be infected would extend to about November 3 or 4.

The population of the borough is remarkably stable; while there were certain cases occurring in the townships, they have been included in the census which was carefully made by agents of the State Department of Health. The latter shows that 1343 persons had constantly used the water supply, and these constitute the number who were exposed to infection by typhoid fever from that source. There were 229 cases developed during the entire epidemic, of which but 4 cases were shown to have been secondary.

A mixed vaccine was used, made according to the following formula:

	Syringe 1.	Syringe 2.	Syringe 3.
<i>Bacillus typhosus</i>	500	1000	1,000,000,000
<i>Bacillus paratyphosus</i> A	250	500	500,000,000
<i>Bacillus paratyphosus</i> B	250	500	500,000,000

The organisms used were strains in use in the United States Army Laboratories. The inoculations were given every nine or ten days.

The tabulation of the use of vaccine shows that of the 1343 who were definitely exposed to the infection, 761 (or 56.56 per cent.) persons received inoculations, while 582 (or 43.32 per cent.) persons were not vaccinated. If the total number of persons exposed after deducting 127 persons already sick is used as a basis it would be shown that 62.5 per cent. of those exposed but apparently well at the time of the first inoculation received vaccine.

The first inoculation was given during the week beginning October 14, and while all were not inoculated on the first day, the statistics which are presented are based upon the relation of inoculation to the individual dates of onset.

AGE AND SEX. The study of the age and sex of those inoculated is of some interest; the age periods of the greatest number of persons vaccinated were between fifteen and thirty-five years. However, the predominant age in relation to the morbidity was between five and twenty years. This maximum morbidity occurring at a relatively early age, as contrasted with the age period usually considered most susceptible, was an important factor in the study of the susceptibility of the community as a whole. The wide latitude of susceptibility is shown by the ages of those who were ill, ranging from two and one-half to eighty-four years. It should be noted that this community had always been typhoid-free, and that acute bacillary disease of the intestinal tract was relatively unknown. The ages of those vaccinated conformed to this wide range of susceptibility, ranging from one and one-half to seventy-nine years. 373 (or 49.2 per cent.) presented for vaccination were males, while 388 (or 50.8 per cent.) were females.

RELATION OF TIME OF VACCINATION TO MORBIDITY. Of the 229 cases, 127 developed the disease prior to October 14, the date of first inoculation, and 102 became ill subsequent to that date.

The morbidity in relation to the total number of persons vaccinated and unvaccinated shows:

Number of persons vaccinated	761
Number of persons vaccinated but developing typhoid fever	37 (or 4.86%)
Number of persons not vaccinated	582
Number of persons not vaccinated developing typhoid fever prior to October 14	127
Number of persons not vaccinated and well prior to October 14 . .	455
Number of persons not vaccinated developing the disease subsequent to October 14	65 (or 14.28%)

That is, of all persons who remained well up to and including the date of first inoculation, 4.86 per cent. of the vaccinated and 14.28 per cent. of the unvaccinated developed the disease.

The first inoculation was given on October 14 and the third on November 3. Between these dates, 35 of the 37 onsets in vaccinated persons occurred at varying periods. The inoculation period of those last infected corresponds to the limitations of these same dates, and would extend to November 4.

MORBIDITY AND MORTALITY OF THE VACCINATED. The clinical evidence of typhoid fever in the 37 vaccinated persons occurred in 28 persons after the first inoculation, in 7 persons after the second, and in 2 persons after the third inoculation.

The clinical features in the vaccinated are of importance and the analysis of 19 cases shows the following:

1. *The Onset.* This was prolonged in every case; the only evidence of acceleration of onset was the appearance of a recognized temperature (which became continuous) shortly after vaccination in a majority of the cases.

2. *The Type of Temperature.* There was no apparent modification; in all cases it was of continued type, the regular morning remission being noted in the majority, and the defervescence was by lysis.

3. *The Duration of Illness.* The average for all not having a relapse was twenty-eight days, the shortest twenty-one days, the longest thirty-one days.

4. *Relapse.* This occurred in 6 (or 31.5 per cent.); in 1 case the entire period of illness lasted over one hundred days.

5. *The Complications.* Among these may be mentioned the effect on the nervous system, 5 showing marked delirium. Acute nephritis followed in 2 cases; this cannot be accounted for by reason of previous nephritis or any other factor than the present illness. Intestinal hemorrhage occurred in 3 cases, thrombosis and phlebitis in 2 cases, and a lobar pneumonia in 1 case.

6. *The Mortality.* There was one death of those vaccinated, a mortality of 0.27 per cent. This patient, a female, aged seventeen years, received one inoculation on October 18. Date of onset, October 21; the patient was confined to bed November 5; pneumonic dulness, lower lobe, right lung, November 12; severe intestinal hemorrhage November 16; death on November 21. In contrast with this there were 17 deaths among the unvaccinated, a mortality of 8.85 per cent. The case mortality during the entire epidemic was 8.29 per cent.

These results are not in agreement with the statement made by Spooner that the course of the disease is modified by prophylactic inoculations of vaccine. Nor is it possible to compare these statistics with the work of Cullinan or Spooner. The former gives the statistics of an epidemic continuing over a long period of time, the percentage of positive and negative results being for two classes of individuals. Spooner's work, while more useful as a means of comparison, does not state the relation of the use of vaccine to the use of the transmitting agent.

The argument in favor of the use of vaccine under these conditions is found in the relative percentage of morbidity of vaccinated and unvaccinated, strengthened somewhat by the fact that the larger proportion of the population received vaccine and the smaller percentage of those developing typhoid occurred in the vaccinated.

However, it should be noted that the usual morbidity in water-borne epidemics varies from 2 per cent. to 10 per cent. of the population. That portion of the morbidity occurring prior to the first use of vaccine in Troy was 9.45 per cent., and the total morbidity was 17 per cent. of the population. Over 58 per cent. of those becoming ill after October 14 show onsets within five days of that date. Hence the conclusion is formed that some other factors were of importance in determining the value of vaccine in the epidemic—namely, the time, degree, and continuance of pollution and the broader problems of susceptibility of the exposed and virulence of the infecting microorganisms. It would not seem advisable to place too much value upon the use of vaccine until these factors had been considered.

It is obvious that the results obtained would vary with every epidemic reported, as the factors relating to pollution and the continuance vary. However, the underlying principles in the use of vaccine would be the same.

The 2 cases developing typhoid fever after the end of the incubation period for all cases infected are of importance. The first case, E. A., female, aged twenty-seven years, graduate nurse, received the first inoculation on October 25 and the second on November 4. The first subjective evidences of the disease were noted on November 5. This was followed by the development of temperature which ran a normal course, subsiding by lysis to normal on November 25. The recrudescence appeared on December 1 with a temperature course lasting for two weeks. The patient gave the usual history and clinical picture of typhoid fever. It is altogether probable that this patient was infected just prior to the disinfection of the water supply; she may have been a secondary case, although there are reasons to exclude the latter factor.

The second case, H. B., a male, aged twenty-three years, is of greater interest. He received his first inoculation on October 16, the second on October 26, and the third on November 10. The onset of temperature occurred eight days later, November 18, and ran the usual typhoidal course, returning to normal by lysis on December 4. During the course of the disease he suffered slight intestinal hemorrhage, but there were no other evidences of complications, and recovery was uninterrupted and complete.

Even if the incubation period had been the maximum of thirty days noted in a small percentage of cases, his onset would date four or five days subsequent to the abatement of the source. Regardless as to what time and where he acquired his infection, the development of the disease in its typical form, occurring eight days after the third inoculation, would suggest that antibodies had not been created in sufficient amounts to give protection.

DETERMINATIVE USAGE. The value of an antivaccine of this type during the course of an epidemic seems to be determined by

the time of its use in relation to many factors, of which the principal ones are as follows:

1. *The Abruptness of Pollution of the Transmitting Agent.* With the common agents—namely, water, milk, and ice-cream—there is the widest latitude for a long-continued or an abrupt pollution to occur. It is during epidemics in which these are the agents that the use of a vaccine must be most carefully considered. Its use to prevent infection through all other agencies is apparently as valuable as its use in military and institutional experience seems to indicate. However, in an abrupt and unrecognized pollution the actual benefits are questionable, and it is far from being proved that it is wise under such conditions to use it until the incubation period of those early infected has ended or until careful exclusion by blood culture indicates that the applicant is not already a potential patient.

2. *The Degree of Pollution.* It is obvious that a small amount of sewage introduced into a large volume of water would lessen the possibility of infecting the users of that supply. If there is a mass pollution of the supply the epidemic tends to assume the explosive character so frequently recorded in water-borne epidemics. Other factors influence the results when the agent is other than water, but the principle is constant. When mass pollution occurs the immediate results are similar to those when the pollution is abrupt, but less concentrated, and the use of a vaccine during the early portion of the epidemic must depend on a careful analysis of each applicant, not only as to his immediate physical condition, but also as to his use of the suspected or known source of infection.

3. *The Susceptibility of those Exposed.* Individual susceptibility is too large a subject to discuss within the limitations or purposes of this article. However, when a community has for a long period used a water supply which is constantly carrying sewage, the individuals seem to develop what has been called by Adams¹¹ an "accustomance" to long-continued and often repeated minimal doses of toxins of the infecting microorganisms. This resistance is not apparent but real. One Pennsylvania town using a known sewage-polluted stream has suffered with endemic bacillary infections for many years. During the past ten years upward of 90 per cent. of those developing typhoid fever have been children. In Troy the high-case morbidity (17 per cent.) and the community history suggest the importance of a community resistance, and it would seem that the results of the use of vaccine would be modified by this acquired resistance.

4. *The Virulence of the Specific Strain causing the Epidemic.* This has been shown to be of importance in many epidemics occurring in Pennsylvania. Two types serve to illustrate its importance.

¹¹ Principles of Pathology.

The mortality as recorded in an epidemic in Indiana County was 14.8 per cent.; the residents were, for the most part, foreign-born and accustomed to the use of promiscuous water supplies. The organisms were transmitted by means of a spring-water supply from cases suffering with a virulent form of the disease. In the Troy epidemic the strain of the bacillus causing the epidemic was recovered from a carrier and the mortality was 8.29 per cent. These two epidemics were water-borne and the abruptness of the onsets and the degree of pollution were similar. The difference in mortality can be explained only by the difference in virulence of the specific strain of the microorganism, and to a less degree the susceptibility of those who were infected.

5. *The Time of Use of the Vaccine in Relation to the Use of the Source of Infection.* This is obviously of the greatest importance. If the infection of patients occurs as the result of a high degree of pollution which has been quickly established it is probable that vaccine prophylaxis will be of no value. However, in epidemics in which there is a low degree of pollution, even if the pollution occurs abruptly, the insusceptibility of many of those exposed will prolong the incubation period; in others, the infection may occur late during the course of the epidemic, and, in addition, there are unexplained cases occurring over a long period after the epidemic has subsided. After exercising care to analyze each applicant's case the prophylactic use of vaccine may seem advisable in these latter cases.

6. *The Number of Bacteria or the Amount of Vaccine Used.* In no other condition does the number of microorganisms or the amount of vaccine assume the same importance as in persons who are in the prodromal stage of the disease. It is, at least theoretically, unwise to give maximum prophylactic inoculations to such persons. It is desirable, during an epidemic (if the patient is not in the prodromal stage of the disease), to establish immunity as quickly as possible and with the least number of inoculations. This implies an increase in the dosage, which is opposed to the underlying principles of vaccine immunization. The production of active immunity by the formation of specific antibodies cannot be done in a hurry. The use of larger doses than are used at present has already been shown to be followed by undesirable phenomena in healthy persons. Hence for two very good reasons it would not seem advisable to give maximum doses to a healthy person and much less to one who is a potential case of typhoid fever.

7. *The Possibility of the Existence of a "Negative Phase,"* which was first discussed by Wright,¹² has not been absolutely eliminated from consideration, although Leishman states that the dangers

¹² British Med. Jour., January 30, 1897.

are more theoretical than real. Russell¹³ quotes Cullinan, Leishman, and the "consensus of opinion of the 1907 International Congress of Hygiene" to prove its unimportance. Leishman¹⁴ also states that the most important evidence must come from actual practice rather than from laboratory experiment. The "actual practice" in Troy indicates the inadvisability of adding large doses of toxins to patients whose poise between susceptibility and resistance already hangs in the balance. If an interval of decreased resistance does exist between inoculation and the formation of antibodies it is of the greatest importance in those who have been exposed to infection. The first opinion entertained after studying the Troy cases was in agreement with Spooner,¹⁵ who suggests "an acceleration of onset" in the infected vaccinated case. A closer analysis fails to confirm his opinion; the prolonged incubation period in all cases, the delayed onset until many days after the second inoculation in 4 cases and until seven days after the third inoculation in one case, outweighs the appearance of the occurrence of clinical evidences of disease in 11 cases coincident with the first inoculation. On the other hand, the negative phase is believed not to last more than "several days" (Wright) unless it is prolonged by large doses. While no positive statements as based on the Troy cases can be made it is to be inferred that resistance to the infecting bacilli had been temporarily lessened.

8. *The Types of Vaccine* so far used during epidemics have been limited to strains of the *Bacillus typhosus* only. In Pennsylvania epidemic experience has sufficiently justified the very certain belief that the paratyphoid fevers and, to a certain extent, infections by organisms of the Gaertner type are endemic and may be almost as great a menace as are infections by the *Bacillus typhosus*.

The studies of atypical cases in Coatesville, Iselin, and elsewhere indicate the prevalence of mixed infections, particularly when water-borne. For this reason vaccines which include other forms would seem to be of greater value than a vaccine including only the *Bacillus typhosus* strains.

Lyons¹⁶ studied paratyphoid vaccine therapy after observing that an attack of typhoid fever and the use of antityphoid vaccine failed to protect against paratyphoid fever. Kabeshima¹⁷ inoculated 300 men with mixed vaccine containing typhoid and paratyphoid strains, because the hospital admissions for three years showed paratyphoid fever was eight times in excess of typhoid fever. The results of his observations were apparently highly satisfactory.

Riesman,¹⁸ in a recent report to the College of Physicians of

¹³ Boston Med. and Surg. Jour., January 5, 1911.

¹⁴ Loc. cit.

¹⁶ New Orleans Med. and Surg. Jour., November, 1911.

¹⁷ Bull. Naval Med. Assoc. of Japan, May, 1912.

¹⁸ Trans. Coll. of Phys., Philadelphia, 1913.

¹⁵ Loc. cit.

Philadelphia, reviewed cases of paratyphoid fever under the suggested title of "entericoid fever," and emphasized the value of mixed vaccine. The absence of a co-immunity between micro-organisms of the typho-colon series was shown in his cases, as all had had typhoid fever within three and one-half to twelve years.

A mixed vaccine of this type in epidemic work has not previously been reported. So far as the prevalence in Pennsylvania is concerned the value of a mixed vaccine in routine immunization is emphasized. In epidemic use it would be limited to those who had not been exposed to the original source of infection.

In a report¹⁹ of this epidemic it was stated that "the use of antityphoid vaccine was an important factor in preventing a number of cases." By this was meant the prevention of secondary cases and the cases which practically always occur in the aftermath of a water-borne epidemic. The latter form an interesting study, since they occur even when engineering interference is prompt and apparently efficient. It may be they are infected from carriers (formed during the epidemic), and should be included among the secondary cases.

The pertinent conclusions from the studies made in this one epidemic indicate the little value antityphoid vaccine has in limiting the number of cases and in modifying the process in the individual case. It would seem since antityphoid serum confers relatively a more immediate and fairly strong immunity that a serum would be of some advantage during such an epidemic. The use of vaccine should be limited to those not already infected, that is, to prevent secondary cases. To this end the individual history and diagnosis by culture would determine its use.

I desire to express my great appreciation to the physicians in Troy for the opportunity to study their cases, and to these same physicians and those from Canton and Towanda who assisted in the administration of vaccine.

A STUDY OF CASES OF ACTINOMYCOSIS.

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A STUDY of the clinical histories and subsequent course of the cases of actinomycosis in the Royal Victoria Hospital during the past twelve years has revealed many features of great interest. The fact that the disease is not uncommon in rural communities,

¹⁹ Hunt, loc. cit.

and that it is frequently mistaken for tuberculosis, or even malignant disease, even by the most astute diagnosticians, renders it advisable to discuss the character of the disease, since an early diagnosis is important if suitable lines of treatment are to be adopted.

The history of the subject may be briefly summarized as follows:

A disease occurring in cattle, in which the chief symptom was swelling of the jaw, was described by Le Blanc in 1826. A similar condition was mentioned by Professor Dick in 1833, and he surmised that the same disease occurred in man. In 1845, Langenbeck described a case of vertebral caries in a young man, the pus from which contained numerous sulphur-like granules. In 1850, Devain described a tumor of the jaw in an ox, the pus from which contained yellow granules similar to those described by Langenbeck. He stated that, microscopically, the characters were neither those of tubercle nor of malignant disease. In 1858, a case in which the thorax was affected was described by Lebert, and similar cases were reported about the same time by Laboulene, Robin and others. A disease known as *mal di rospo* in Italy, in which the prominent symptom was a tumor of the jaw, was studied by Rivolta in 1863, and five years later he discovered rod-shaped bodies in the pus. He was unable to inoculate successfully, but later established the identity of the disease in the horse, dog, and most of the domestic animals.

While isolated cases were discovered after this date, it was not established until 1877 that the peculiar rod-like bodies found in the jaw in tumors of oxen were the cause of the disease.

Bollinger, and his botanical colleague Hartz, of Munich, recognized the parasitic nature of the bodies and gave the name "ray fungus" to them, owing to their radiate appearance. In 1878, Israel described two cases of a new form of mycosis in man, and isolated the fungus from multiple abscesses. The following year Ponfick found the same fungus in a prevertebral abscess, and suggested the identity of the disease in man and in animals. Johne successfully inoculated an ox with the yellow granules. The latter were first studied by Perrocito in 1875, who noted their occurrence in what was considered osteosarcoma of the jaw. In England, Auckland (1899) was the first to meet with a case in man, the liver being the part affected. The disease was studied in animals in the United States by Bellafield, of Chicago, in 1883, and Murphy described similar cases in the human subject shortly afterward. The first case recognized in the human subject in Canada was diagnosticated in the Royal Victoria Hospital, Montreal, in 1900, in a case of persistent lumbar sinus of obscure origin under the care of the late Dr. James Bell, at whose instigation Dr. A. G. Nichols was able to demonstrate the fungus.

Geographical Distribution of the Disease. The environs of Berlin, Germany; the salt marshes of Russia; Italy; Austria; part of England; North America.

In our own cases the remarkable fact was noted that with the exception of three or four cases they all came from locations within a hundred miles of Montreal. One small strip along the St. Lawrence River furnished a large number of our cases, and the other locality was south of Montreal and in the eastern townships. In the city itself several cases have occurred, all in the north or east of the city. The reason lies in the fact that there is a greater opportunity for infection in these localities.

Season. It is a remarkable fact that nearly all our jaw cases come to us between September and January (see List of Cases), while the abdominal and pulmonary cases are usually admitted late in the spring, having, however, complained of symptoms for a considerable period (see List of Cases). This is natural when one considers the mode of infection from grain. The lesion on jaws makes itself apparent earlier, while the deeper abdominal conditions take longer to manifest themselves. In cattle the disease is most common in dry-feeding periods.

Sex. Males are infected much more frequently than females. In our series of 37 cases only 9 were females.

Appendix	1 female out of 13 cases.
Left groin	2 females out of 3 cases.
Cervicofacial	6 females out of 19 cases.
Others	0 females out of 2 cases.

Females usually take better care of their teeth, and are less liable to chew straws, or to be brought into contact with infection.

Age. The youngest case was aged ten years, the oldest, fifty-four years. Most frequently the age was between twenty-five and thirty-five years. The disease is rare in children.

Occupation. Males: farmers, 19; laborers, 5; steam-fitters, 2; clerks, 2; superintendent of car works, 1; electric engineer, 1; bricklayer, 1; grain merchant, 1; millwright, 1; cheesemaker, 1; merchant (country), 1; lawyer, 1.

Race. No race seems immune. All of our cases have occurred among whites, but since negroes are not numerous in the affected region, our own statistics afford us no data under this heading.

Methods of Infection. The organism is widely distributed in nature and is easily isolated from certain grasses. Direct contagion is denied by many observers (Leith). On the other hand there have been cases reported where men have contracted it from animals infected with the disease (Barazac mentions two cases). Finally, at the Royal Victoria Hospital, one of the earliest cases occurred in a nurse who had been attending a case of actinomycosis. The proof for direct infection is not very convincing, but the above case and other suspicious ones render it likely that it does occur at times if the conditions for infection are favorable. There is not much evidence in favor of direct infection from animal

to animal, and there is considerable evidence against it, with one interesting example. Salmon put twenty-two healthy cattle with infected ones for a period of four months and none developed the disease.

Infection by Milk. The mammæ of cattle are rarely infected by the disease. If the disease originated from milk we would expect to see it more frequently in babies, in whom, however, it is exceedingly rare.

Infection by Food. Here also several factors exist which do not permit the probability of infection: (1) The parts affected by the disease are not used for food, and (2) the ordinary process of cooking destroys the organism.

Infection from Plants. There are numerous examples and experiments which go to prove that direct infection from plants can take place. Johnne found a husk covered with fungus in the tonsil of a pig, and several French cases are reported where injuries have occurred while handling grain, followed a few days later by the appearance of the disease.

Conditions Necessary to Infection. Johnne, in 1888, fed animals on food mixed with cultures of the organism, but in no case did the disease develop. It is to be noted that in all our jaw cases of actinomycosis we have never had abdominal infection. The favorite sites of intestinal actinomycosis are the cecum, appendix, and rectum; in the pulmonary cases it is most frequently right-sided, and attacks the base rather than the apex of the lung, in contrast to its kin tuberculosis.

It has been proved by Johnne and others that cattle fed on virulent cultures will not acquire the disease. It seems that the carrier of the microbe must be able to penetrate the surface (chewing straw), or there must be some abrasion present, for example, soft spongy gums around a carious tooth. The proof of this in all our jaw cases lay in the fact that the teeth on the affected side were in bad condition, and that the disease affected either the upper or lower jaw according to the situation of bad teeth. The fact that the presence of an ulcerated surface is needed to permit the entrance of the organism into tissues explains why the disease is more common in the appendix and rectum. According to statistics, there are inflammatory changes and small ulcers, etc., in the appendix in 75 per cent. of healthy adults. Again, in this region the process of movement is retarded; the fecal mass is becoming more solid and remains longer in the area. Solid particles themselves may cause abrasions which permit the entrance of the organism. For the same reasons the rectum is more likely to show superficial ulceration. The reason that ulcer of the stomach is not more often affected is because the acid of the stomach prevents the growth of the organism. In fact, it is rare to see secondary infection of any chronic ulcer by actinomycosis. It seems to

flourish best in acute lesions. It has been reported as occurring in typhoid ulceration.

Infection by Inhalation of Dust While Threshing. Pulmonary infection by inhalation may occur, but this is rare. Israel pointed out that it was impossible without some associated injury to the tissue of the lung. In one case the disease started around a portion of an aspirated tooth, and in another a barley beard was the originator of the focus. Again, in all our pulmonary cases there had been abdominal symptoms previously. In one case the appendix abscess was opened, drained, and healed, and one year later an abscess developed over the thoracic wall, which was opened and drained. The appendix condition had apparently healed up, the mass disappeared, and all that remained was the scar. Again, the fact that it most frequently involves the lower lobe of the right lung is also strong evidence in favor of infection via the appendix—that is, ascending infection. It is not necessary to have a marked appendix lesion to have pulmonary symptoms, but if the appendix were examined in every case of pulmonary actinomycosis we should most likely find some evidence that the organism had gained an entrance to the circulation from that site. In left-sided cases the seat of the original trouble is probably the rectum. In two cases the original trouble was in the groin, in another the abdominal wall. The organism spreads, as stated above, by blood, but occasionally by lymphatics, as in a case of primary rectal infection reported by Bevan, in which the inguinal glands were involved. The fact that injury is necessary for the entrance of the organism is further emphasized by the fact that cattle living on salt marshes which are periodically covered by the sea are more susceptible, the jaw being injured by sand-shells, etc.

Bostrom observed beards of grain in 11 cases. Frequently there is the history that the patient used straws as toothpicks.

An example following an injury to the finger is given by Suchard.¹ The wound was caused by a spike of corn penetrating the index finger. In eight days a small pustule appeared.

Ziemann, in 1883, reports one case of infection occurring through the vagina.

Incubation Period. This varies from a few days, as in our jaw cases, to weeks and months in abdominal and pulmonary cases.

Local Tissue Changes. The organism having found lodgement in the tissues sets up hyaline degeneration in the tissues immediately around. In stained specimens there is a central bright pink homogeneous mass inclosed in a more or less dense collection of round cells (mononuclears). Further away from the lesions we find numerous large spindle cells; and a few giant cells appear, par-

¹ La Presse Médicale, August 15, 1903.

ticularly in the outer zone of infection. There is a new form of connective tissue about the foci of infection, which in cattle is prone to undergo calcification, while in man this change is rare. In the interstices of the new-formed tissue colonies of the streptothrix are found with their attendant zone of inflammation as described above. When there is an excessive production of connective tissue the cases partake of the nature of newgrowth. An overgrowth of streptothrix in one of these interstices leads to break-down and formation of sinuses, or of an abscess. The disease spreads by contiguity and along the blood stream, rarely by lymph channels.

The pus from the cavities is small in quantity and has a peculiar earthy odor, is usually blood-stained, and contains the characteristic sulphur-yellow granules, which in cattle possess a very gritty feel, and are found under the microscope to be colonies of the organism. The central part of a colony consists of a mass of filaments (mycelium) which form a dense felted network. At the periphery there are large pear-like forms which have received the name of clubs; coccus-like forms (probably cross-views of filaments) are also present. The mycelium is made of long thin threads, which are frequently wavy, like spirochetes. They consist of a shred of protoplasm, which shows much fragmentation in old cultures, and at their tip is dichotomous branching. The fragmentation gives the filaments the appearance of chains of streptococci of varying length. They are positive to Gram.

The Clubs. These appear to be the swollen terminal extremities of the filaments. They are more frequently met with in cattle than in man, and are more abundant in chronic cases. They have a pale hyaline appearance, are pear-shaped, and negative to Gram. They are probably degenerative forms, and result from the action of the body juices on the filaments. They are best seen with the low power after crushing the material with 10 per cent. potash under a cover-slip. The central granular mass with arrangements of filaments or clubs around it is then characteristic.

The organism grows with so much difficulty on all ordinary media that cultural methods are of no practical value to the clinician. Lieberman was able to grow the streptothrix on plants, and he also showed that it became attenuated by passing through the animal body (unlike most organisms), and regained its virulence after being grown on plants. This probably explains why infection from one animal to another is rare.

Site of Disease. In domestic animals it is most frequently met with in the jaw, except in Russia, where it is the skin which is most frequently affected. As regards man, the statistics given by Ruräh of 1094 European cases are: Head and neck, 56 per cent.; digestive tract, 20 per cent.; pulmonary, 15 per cent.; skin, 2 per cent.

Our statistics of 37 cases record the following: Cervicofacial, 19; appendix, cecum, and abdominal wall, 13; left groin, 3; left groin, lumbar region, 1; skin, 1.

Clinical Features of the Histories of Our Cases. The clinical history of a disease so varied in its manifestations presents some difficulties in description. Here again it resembles tuberculosis, but is best studied by considering in turn the various regions of the body affected. I will here confine myself to the regions exemplified by our own cases, that is, the jaw, cecum, appendix, and thorax, by giving a short account of actual cases.

1. *Appendix Cases.* In all we have had 13 cases diagnosed actinomycosis of appendix and abdominal wall, 2 of which are doubtful, leaving 11 undoubted cases. Unfortunately the majority of the cases that ended fatally were sent home before death, and with the exception of our first case and Case 10 (see List of Cases), no autopsy, or only a very superficial one, was made. The fact brought out by the cases is the high mortality. We can report only 2 cures. The diagnosis was rarely made before operation, not even until a fistula formed which occurred in 9 cases out of 11 (Cases 2, 3, 4, 5, 8, 9, 10, 11, 13), from the pus of which the organism was isolated. Lung and liver complications occurred in 8 cases (1, 2, 5, 6, 8, 10, 12, 13). Cases 5 and 13 show the liability of the disease to completely heal at the site of inoculation and reappear in other localities far removed.

Clinical Features of Appendix and Abdominal Wall Cases. Males are more affected than females, 12 to 1. The patients usually come to the hospital between January and May, differing in this respect from jaw and cheek cases, which usually come to the hospital between September and January.

The initial symptoms are, as a rule, like those of acute appendicitis, differing from the ordinary form in that the patient never completely recovers after the attack. Vomiting is not so frequently present with the attacks, while diarrhea is much more constant. A peculiar hard mass soon forms, and flexion of the psoas muscle is often early and marked. In fact, the difficulty in straightening the leg is frequently noticed before the mass is discovered. As the disease progresses jaundice not infrequently develops, and later on loin and subphrenic abscesses appear, with final involvement of the lungs. If operated upon the character of the muscular infiltration with small amounts of pus may point to the diagnosis, but even then the surgeon may fail to appreciate the condition until the later developments of fistulæ and sinuses which will not close, but continue to discharge pus-containing yellow granules, leads for the first time to the discovery of the organism.

2. *The cervicofacial cases* were 19 in number. The after-history was particularly difficult to trace, but some of these patients would probably have returned to the hospital for treatment if they had

had a recurrence. Cases 1, 2, 5, 15 could not be traced. Cases 13 and 14 showed no improvement. In Case No. 4 the organism was doubtful. Case No. 9 is particularly interesting from the chronicity; began in 1904, and from then until October, 1911, had 100 operations, consisting of opening, curetting, etc.; died, June, 1912, from nephritis, after having nine months' freedom from disease. The cause of death was recorded as due to excessive chloroform, ether, and perhaps potassium iodide, which he took for long periods (60 gr., t. i. d.).

Females were affected in 6 cases; the remainder were males. In all cases decayed teeth were present. Patients began to have trouble in the early fall, coming to the hospital between September and January.

The jaw and cheek cases have certain points in their history and clinical course which are almost characteristic: (1) There is usually a history of bad teeth, the appearance of a gum-boil near the decayed tooth which will not heal; (2) the tooth being extracted, the abscess is better for a while, but reopens, until finally the process involves the cheek, and as it comes near the surface the skin over it has a characteristic color—a dark, glossy, purplish red. The chronicity of the affection is well exemplified by a case that came first in 1902 (Case No. 9 cervicofacial series) and has been coming at intervals every year since.

3. *Clinical Features of the Groin Cases.* The cases occurred in 2 females and 1 male. The females both recovered and we were unable to trace the after-history of the third case. So far as our limited experience reaches, it is relatively good as regards prognosis. There is nothing of much interest to note in the clinical symptoms other than the fact that in all our cases abdominal symptoms were present, and a doctor was only consulted when a mass was recognized. In Case 1 urinary symptoms were complained of, but operation revealed no connection between bladder and abscess cavity. Unfortunately in none of these cases was a rectal examination made, and there was no mention of hemorrhoids or fissure in the case reports. In any event it is probable that the seat of infection was from a fissure or ulcer in the anus or rectum, and to explain its occurrence in the left groin, lymphatic extension from the anus to the groin is the only intelligible way of explaining it. This method of extension is rare, but such cases have been reported (Bevan).

4. *The pulmonary lesions* as stated above may begin from an air infection, provided there is the necessary injury, but in far the largest number of cases the primary lesion is in the appendix, although the disease may be entirely manifested in the lungs. When occurring in the lungs we have to differentiate it from tuberculosis. The points are that in actinomyces there are usually some transitory gastro-intestinal symptoms of rather acute char-

acter. The base rather than the apex is affected. Hemoptysis is the exception. Jaundice is frequently present. The organism is found in sputum. Infection travels from below up, not *vice versa*.

5. *Our one skin* case began as small vesicles, which coalesced to form a chronic ulcer with ragged edges and sloughy base. The organism was never isolated. Excision. Patient cured.

PROGNOSIS. The prognosis varies with the situation and extent of the lesion and the initial virulence. A large lesion and the relation to important structures are bad factors. Jiron gives the following statistics of mortality: Face and neck, 11 per cent.; thorax, 83 per cent.; abdominal, 71 per cent.; cerebral, 100 per cent.

Our cases show better results as regards face and neck, as mortality is almost *nil*, but our thoracic and abdominal cases have been almost invariably fatal, over 95 per cent. having died.

TREATMENT. When possible, as in the case of the cheek, total excision is best; in other places the routine is: Opening, followed by curetting, washing the cavity with weak solution of iodine, packing with iodoform gauze, and giving large doses of potassium iodide. The iodide does not act on the organism itself, but seems to have some effect on the tissues, which enables them to overcome the disease (Prutz). When iodides have failed, copper sulphate and various other remedies, including x -rays, have been used, but nothing so far replaces the iodides. Our experience here is that x -rays are distinctly harmful, causing a spread of the disease in both actino- and blastomycosis.

SUMMARY. 1. Actinomycosis is a more common affection than is generally believed, especially in rural communities.

2. It is frequently mistaken for tuberculosis or newgrowth.

3. There are certain characteristics about the cases from each locality which lead to suspicion of the nature of the disease.

4. The usual situations are the jaw, cheek, appendix, and cecum, with thoracic involvement.

5. Infection cannot occur without a lesion in the skin or mucous membrane.

6. Jaw cases are more frequent in the fall of the year, abdominal and thoracic cases in winter and spring.

7. The onset is often acute.

8. Abdominal actinomycosis shows peculiar liability to fistula formation and tendency to heal at the site of the initial lesion, appearing elsewhere.

9. Abdominal and thoracic forms show high mortality. In skin and jaw cases the prognosis is satisfactory.

10. Diagnosis of primary pulmonary actinomycosis, even in the absence of abdominal symptoms, must remain doubtful without careful postmortem examination.

11. In all our pulmonary forms there has been a previous history of abdominal symptoms.

12. Excision is the best method of treatment where possible. Otherwise, free incision, curetting, washing with weak iodine solution, packing with iodoform gauze, associated with large doses of potassium iodide internally, should be adopted.

13. The relation between cattle and human actinomycosis is closer than that between human and bovine tuberculosis.

In conclusion, I desire to thank Dr. O. C. Gruner, chief of the pathological department of the Royal Victoria Hospital, for his assistance in the preparation of this paper, particularly in the postmortem work.

APPENDIX SERIES.

CASE 1.—Farmer, male, aged twenty-two years, residing, at Ontario. Seat of disease, liver. Duration of symptoms before admission, three months. Admitted, March, 1900.

Chief Features of Illness. Began with loss of appetite; feeling of malaise; crampy pain in abdomen; two months ago slight cough developed, with some expectoration. Temperature at night 103°. One week ago sudden onset of severe coughing, with profuse greenish-yellow expectoration. This was followed by slight improvement. Patient had had what was diagnosticated as pleurisy twelve years previously.

Treatment. Exploratory puncture revealed only blood-stained serum. Tenth rib resected. Lung adherent to diaphragm. Little pus found. Drainage.

Result. Died.

Remarks. Clinical diagnosis made at operation never confirmed by isolating organism until autopsy was made. Notes of autopsy: First case of actinomycosis positively demonstrated in Canada; was diagnosticated primary actinomycosis of the liver because the largest mass was there and because no primary focus was found elsewhere. The appendix was found in the pelvis covered with adhesions. Microscopic diagnosis was chronic appendicitis. This was the probable source of infection, but was not considered so at the time of autopsy.

CASE 2.—Farmer, male, aged fifty-four years, residing at Province of Quebec. Seat of disease, retroperitoneal glands. Duration of symptoms before admission, two months. Admitted, April, 1900.

Chief Features of Illness. Sudden onset of pain in abdomen, with diarrhea. No nausea or vomiting. Attack lasted four days. In short period of time had several similar attacks. Thigh became flexed on abdomen. Complained of pain in sacral region and down thigh. On examination, tender mass was felt in lower right quadrant.

Treatment. Abdomen opened as for appendix. Considerable necrotic tissue in region of appendix. Drained.

Result. Died at home. No autopsy.

Remarks. Several operations performed to close sinuses without avail. Appendix never located.

CASE 3.—Farmer, male, aged forty-five years, residing at Ontario. Seat of disease, appendix and cecum. Duration of symptoms before admission, one month. Admitted, November, 1900.

Chief Features of Illness. Pain in right ileocecal region, coming on suddenly without apparent cause. Shortly afterward, difficulty in walking. Thigh flexed. Appearance of mass. Lost thirty pounds in weight.

Treatment. Incision parallel to crest of ilium, $1\frac{1}{2}$ cm. above. Muscles present peculiar cartilaginous appearance. Little bleeding. Small amount of pus. Drainage. Potassium iodide.

Result. Died at home.

Remarks. Appendix could not be located. No lung complications.

CASE 4.—Farmer, male, aged thirty-eight years, residing at Province of Quebec. Seat of disease, appendix and cecum. Duration of symptoms before admission, three months. Admitted, August, 1902.

Chief Features of Illness. Sudden onset of pain in right iliac region. No vomiting. One week later appearance of mass in right iliac region and flexion of thigh. All symptoms increased on extension of leg. Remained in bed for three weeks, then got up. Lump remained, and gradually increased. Symptoms subsided. Has been moving about. Leukocytes, 6400. Lately complains of pain down front of thigh. Examination reveals a tender hard mass in lower right quadrant.

Treatment. Appendix lying behind cecum was broken off and removed. Two small seeds found in appendix. Drainage. Fistula formed.

Result. Died at home.

Remarks. Several operations performed to close fistula. Seeds in this case were probably conveyors of infection. Organism never isolated from seeds. Appendix showed small ulcerations of mucosa. Walls thickened and friable. Was diagnosticated acute appendicitis on chronic interstitial. The condition was not suspected until fistula formed, and then the organism was found in the pus.

CASE 5.—Farmer, male, aged thirty-six years, residing at Ontario. Seat of disease, appendix. Duration of symptoms before admission, two months. Admitted, April, 1903.

Chief Features of Illness. Sudden attack of sharp abdominal pain lasting several hours, replaced by dull ache in right lower quadrant. No vomiting or diarrhea. Leukocytes, 16,000. Flexion

of thigh, and mass palpable. Some loss of weight. Slight jaundice. Readmitted in August. Pain in right shoulder and in upper right quadrant. Jaundiced at intervals. Liver dulness increased. Evidence of fluid in right base. Some cough and expectoration.

Treatment. Appendix incision. Abdominal walls infiltrated. Large abscess opened into. Loin drain established. Sinus remained. Discharged from the hospital in June.

Result. Died at home.

Remarks. Peritoneal cavity apparently normal. The old lesions had apparently cleaned up, the disease existing only in tissue of abdominal wall.

CASE 6.—Schoolboy, aged thirteen years, residing at Province of Quebec. Seat of disease, appendix, liver, and pleura. Duration of symptoms before admission, three months. Admitted, November, 1906.

Chief Features of Illness. Acute attack of appendicitis. No vomiting. Remained in bed one week, but never completely recovered. Several similar attacks. Patient walked with slight limp. Right pleural cavity contained fluid. Cough and expectoration.

Treatment. Ninth, tenth, and eleventh ribs resected. Only a small amount of blood-stained fluid. Discharged from the hospital in a critical condition.

Result. Died.

Remarks. No abdominal operation or autopsy. This patient was sent to the hospital for the lung condition. A diagnosis of empyema was made. The abdominal condition was overlooked; at the hospital the relation between the two conditions was noted.

CASE 7.—Farmer, male, aged fifty-one years, residing at Province of Quebec. Seat of disease, appendix. Duration of symptoms before admission, one month. Admitted, September, 1907.

Chief Features of Illness. Sudden onset of abdominal pain, with chilliness. No vomiting. Next day seen by the doctor, who discovered hard mass in right iliac fossa. Loss of weight had been considerable.

Treatment. Refused operation.

Result. Not known.

Remarks. Could not find out about patient.

CASE 8.—Millwright, male, aged forty-two years, residing at Montreal. Seat of disease, appendix and lung. Duration of symptoms before admission, five months. Admitted, February, 1912.

Chief Features of Illness. Began with an attack described as inflammation of bowels, with some vomiting. Remained in bed three days and about house five weeks. Never became completely well. Three weeks later developed pain in thorax along costal margin. Doctor diagnosticated pleurisy. One night sudden onset

of severe coughing, with considerable expectoration of greenish color, foul odor. No hematemesis. Quantity of expectoration gradually diminished. Few weeks before admission appearance of abscess in right loin. Examination of thorax shows increase of liver dulness, with diminished breath sounds and resonance over whole of right side as high as third rib. X-rays showed the diaphragm unusually high on right side and completely fixed.

Treatment. Abscess in loin opened and drained, packed with iodoform gauze. Potassium iodide by mouth. Sinus led up over the ribs toward thorax. Washing with iodine. Small abscess opened over the tenth rib on right side in anterior axillary line. Several attempts made to close lumbar sinuses by curetting, but finally fecal fistula developed.

Result. Died at home.

Remarks. No autopsy.

CASE 9.—Housewife, female, residing at Ontario. Seat of disease, appendix. Duration of symptoms before admission, one year. Admitted, January.

Chief Features of Illness. Complained of headache, distress in right groin. Small abscess pointed to right iliac region. Opened in June by doctor outside, and appendix removed. Pus evacuated. Abscess healed for short time, reappeared since. There remained a discharging sinus on entrance to the hospital.

Treatment. Abdomen when opened contained straw-colored fluid. The general peritoneal cavity was free. Small sinus leading down to appendix was curetted. Abdomen closed. Sinus packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. At first thought origin was from genitalia. Diagnosis not made until fistula developed.

CASE 10.—Clerk, male, aged eighteen years, residing at Vermont. Seat of disease, appendix and abdominal wall. Duration of symptoms before admission, six months. Admitted, April, 1912.

Chief Features of Illness. Onset of pain in epigastrium, with slight nausea and vomiting. Patient remained in bed five weeks, the pain gradually subsiding, but never completely disappearing, and later felt entirely in right lower quadrant. Fever during this time continuous. Diagnosis of typhoid made by doctor. Condition of patient improved, and was allowed up. Shortly after, swelling appeared in the right lower quadrant. Leg became flexed and pains became severe, extending down right leg. No vomiting or diarrhea. Patient operated upon on admission to the hospital. Incision in appendix region. Muscle much infiltrated. Appendix never found. Wound packed with gauze. Patient discharged, with sinus still persisting (May). Readmitted in June. Improved for short time after leaving the hospital, then gradually became worse. Ten days before second admission to

the hospital, sudden chill followed by profuse sweats, high temperature, cough and expectoration. Second operation, June 11, over gall-bladder region. Liver enlarged, covered with lymph over region of falciform ligament.

Result. Died June 17, during attack of severe dyspnea.

Autopsy. Thorax: Pleural cavities filled with clear fluid. No adhesions. Lungs emphysematous. Cut surface edematous and consolidated throughout; very friable. Scattered throughout and particularly numerous beneath the pleura, were numerous firm, gray nodules about the size of a split pea, many of them broken down in the centre, forming small cavities containing pus.

Peritoneal cavity: Free from fluid. Appendix short, thick, firm, showing numerous adhesions about. Mesenteric and lumbar glands enlarged. Mesentery normal in appearance, showing no evidence of thrombosis. Appendix measured 4.5 cm.; small, conical in shape; serosa roughened and granular from old adhesions; tip obliterated. A section was composed entirely of a layer of dense fibrous tissue; at the proximal extremity the lumen was increased in size; cavity filled with pus of yellowish color, containing one or two sulphur-like granules, in which rather atypical actinomyces were discovered. The clumps were small and much fragmented. In the walls of the appendix itself no actinomyces were demonstrated. In a small abscess at the lower end of the cecum a few thread-like forms were seen, but no definite clubbed or branching processes were discovered. Similarly, scrapings from the bases of small superficial ulcers of the cecum near the cecal valve, showed similar forms.

Liver: Enlarged. At the attachment of the falciform ligament some purulent lymph was noted over a thickened capsule.

Gall-bladder: Normal. Portal vein large. Walls smooth. No evidence of thrombosis. Along its course, however, the main lesion of the organ was noted. Along the right portal, shortly after its origin, a large yellow semisolid area occurred completely surrounding vessel and showing extensive necroses of liver cells for some distance.

CASE 11.—Superintendent of car works, male, aged forty-seven years, residing at Nova Scotia. Seat of disease, appendix. Duration of symptoms before admission, one year. Admitted, January, 1908.

Chief Features of Illness. At first complained of indefinite pain in lower half of abdomen, with loss of appetite. Slight diarrhea. Typhoid fever diagnosticated. Remained in bed two weeks. On getting up found thigh flexed; unable to straighten it. Mass discovered in right lower quadrant. One month ago had a severe attack of pain, accompanied by vomiting. Incision made in mass; small quantity of pus escaped. Wound would not heal. Abscess appeared in loin. Lost weight.

Treatment. Incision in abscess; gauze packing. Potassium iodide internally.

Result. Died one month after leaving the hospital.

Remarks. No evidence of liver or lung complications. No autopsy.

CASE 12.—Student, male, aged ten years, residing at Montreal. Seat of disease, abdominal wall. Duration of symptoms before admission, six weeks. Admitted, February, 1908.

Chief Features of Illness. Onset similar to acute attack of appendicitis with crampy pains particularly in lower right quadrant radiating into loin. Bowels constipated. No vomiting. Right lower quadrant more prominent than rest of abdomen; a tender firm mass, which apparently only involved abdominal wall.

Treatment. Incision into mass. Tissue hard, almost cartilaginous. Little bleeding or pus. Condition entirely extraperitoneal. Potassium iodide.

Result. Cured.

Remarks. The organism in this case was never isolated.

CASE 13.—Clerk, male, aged twenty-five years, residing at Montreal. Seat of disease, appendix and wall of thorax. Duration of symptoms before admission, five years. Admitted, September, 1907.

Chief Features of Illness. Appendix removed five years ago. Fecal fistula developed and did not close for about a year, during which time a small quantity of blood-stained serum exuded. One year later a mass on the right side of the thorax appeared, which broke through the skin, leaving a sinus which has discharged at intervals for the past four years. On entrance to the hospital the appendix scar was healthy and the abdomen quite free. A small sinus was found over the lower part of the thorax in the middle axillary line.

Treatment. Incision along the sinus, which did not go through the parietal wall. Cured. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Here is a definite case of the entrance of the organism via appendix, which later healed and infection was still active in the thorax.

LEFT LOIN AND THORAX.

CASE 1.—Farmer, male, aged thirty-one years, residing at Montreal. Seat of disease, thorax, lumbar region. Duration of symptoms before admission, six months. Admitted, March, 1906.

Chief Features of Illness. Six months previously had an injury to the left side. Shortly after a small, painful mass appeared over the tenth rib in the middle axillary line. Incision by local doctor.

Small amount of pus evacuated. No loss of weight, cough, or expectoration. Readmitted in June, 1906. Small abscess near old scar. By this time some cough and expectoration. Evidence of thickened pleura over left base. Readmitted in January, 1908. Sinus well opened up. Cured down to region of 12 D. V. In February left leg became flexed; mass appeared in loin.

Treatment. Excision of ninth and tenth ribs, both of which were apparently normal. A small sinus tracked into the pleural cavity, running in toward the spine. Cured, packed with gauze. On readmission in June, cured; no evidence of dead bone; disease seemed situated only in soft tissues. Potassium iodide given; iodide gauze packing. On readmission in January, 1908, packed with gauze. Potassium iodide internally.

Result. Died January, 1907.

Remarks. Autopsy at home incomplete. Actinomycosis found in pus, but never in sputa. Great emaciation, with deep yellow color of fatty tissue. Pleura thickened at base and contained a small amount of blood-stained serum. The sinus in loin and chest wall did not go deep but seemed quite superficial, leading down in case of thorax to the excised ribs.

CERVICOFACIAL SERIES.

CASE 1.—Bricklayer, male, aged thirty-seven years, residing at Montreal. Seat of disease, jaw and cheek. Duration of symptoms before admission, one year. Admitted, October, 1908.

Chief Features of Illness. Small mass appeared in the cheek on the right side near angle of the jaw. Lanced. Healed. Shortly afterward another appeared. Treated similarly and healed. Again near angle of jaw another mass appeared, with characteristic purplish skin over it, discharging a small amount of blood-stained pus.

Treatment. Incision. Curing. Packing with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Not diagnosed for some time, until finally the ray fungus was isolated.

CASE 2.—Steamfitter, male, aged twenty-nine years, residing at Montreal. Seat of disease, jaw. Duration of symptoms before admission, three months. Admitted, October, 1908.

Chief Features of Illness. Small firm nodules near decayed molar of lower jaw. Swelling involved cheek; softened, with characteristic color of skin over it.

Treatment. Excision. Tooth extracted. Potassium iodide.

Result. Cured.

Remarks. Patient never had any further trouble six months after operation.

CASE 3.—Farmer, male, aged forty-four years, residing at Ontario. Seat of disease, submaxillary region. Duration of symptoms before admission, two months. Admitted, November, 1908.

Chief Features of Illness. Small tumor in submaxillary region just in front of angle of jaw. Gradually increased in size. Skin over it became purplish. Mass seemed to have no connection with mucous membrane of mouth. Lower teeth decayed.

Treatment. Teeth extracted. Mass excised.

Result. Cured.

Remarks. No further trouble.

CASE 4.—Farmer, male, aged thirty-one years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, two years. Admitted, December, 1908.

Chief Features of Illness. Neuralgic pains of upper jaw. Four months later abscess appeared. Incision; portion of dead bone removed. Attacks recurred. Several operations, curetting, etc. Small sequestrum removed.

Treatment. Incision. Drainage. Packing with gauze.

Result. Cured.

Remarks. Organism never found. This case looks more like active osteomyelitis than actinomycosis.

CASE 5.—Electrician, male, aged twenty-two years, residing at Saranac Lake. Seat of disease, cheek. Duration of symptoms before admission, three years. Admitted, May, 1909.

Chief Features of Illness. Small mass appeared near left molar from which a little pus oozed out. Tooth extracted and abscess healed. In region of old abscess the cheek became involved. Tooth in neighborhood, which was in bad condition, removed. Mass softened. Sinus formed. Skin was the characteristic color.

Treatment. Mass excised. Potassium iodide internally.

Result. Cured.

Remarks. Unable to trace patient.

CASE 6.—Merchant, male, aged twenty-nine years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, one month. Admitted, November, 1909.

Chief Features of Illness. Pain in right lower jaw. Small hard mass appeared in front of angle. Two weeks later face swollen. Mass firm. No evidence of fluctuation. Skin over it reddish purple color.

Treatment. Incision. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Small quantity of blood-stained pus showed granules.

CASE 7.—Farmer, male, aged thirty-one years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, one year. Admitted, August, 1905.

Chief Features of Illness. Swelling of the cheek over the malar bone. A small sinus formed discharging pus into the mouth. Involved the cheek. Opened on the inner side, but still would not heal.

Treatment. Roots of teeth extracted. Free incision and curetting from outside. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Two years after was well.

CASE 8.—Male. Seat of disease, cheek. Duration of symptoms before admission, six months. Admitted, April, 1905.

Chief Features of Illness. Wore plate which did not fit well. Near root of old wisdom tooth, small abscess formed. Tooth extracted. Condition improved. Finally cheek became very much swollen again with purplish discoloration of skin.

Treatment. Excision of mass. Potassium iodide internally.

Result. Cured.

Remarks. No further trouble.

CASE 9.—Lawyer, male, aged twenty-four years, residing at New Brunswick. Seat of disease, jaw. Duration of symptoms before admission, three months. Admitted, April, 1904.

Chief Features of Illness. A small abscess appeared opposite the molar teeth (lower). Incised. A small quantity of pus evacuated. Cavity closed. Two weeks later another similar one appeared. This time it quickly involved the cheek. Central portion soft, dark, reddish-purple in color. The surrounding parts firm, infiltrating. Incision made through cheek down to jaw. A small sequestrum removed. In June reëntered the hospital, with large fluctuating area in front of old scar. Skin over it a dark purplish color. Tender. No glandular involvement. Abscess appeared in right side of neck, also another on left cheek.

Treatment. Incision. Sequestrum removed. Wound healed. On readmission incision along inferior border of jaw; drained. Incision, packed with gauze. Potassium iodide internally. X-rays had a decidedly bad effect; small abscess seemed to form more quickly. Protonuclein, t. i. d.

Remarks. Early diagnosis of acute osteomyelitis. Later actinomyces found. This patient was operated on in all about one hundred times in various parts of the country. The disease extended down both sides of neck. The last operation occurred on October 11, and from that time on he was entirely free from the disease up to the time of his death, which occurred in June, 1911. Death from nephritis, due perhaps to ether-chloroform, or possibly excessive potassium iodide treatment, 60 gr., t. i. d.

CASE 10.—Nurse, female, aged twenty-five years, residing at Montreal. Seat of disease, jaw and cheek. Duration of symptoms before admission, one year. Admitted, October, 1904.

Chief Features of Illness. Small abscess appeared opposite the second molar at the junction of the cheek and the jaw. Discharged small amount of pus at intervals. Cheek finally involved. Characteristic discoloration of skin.

Treatment. Tooth extracted. Mass excised. Potassium iodide internally.

Result. Cured.

Remarks. This nurse attended patient No. 9.

CASE 11.—Wife of a farmer, aged twenty-two years, residing at Ontario. Seat of disease, jaw and cheek. Duration of symptoms before admission, one month. Admitted, October, 1904.

Chief Features of Illness. Began as firm nodule near lower right wisdom tooth. Incised; a small quantity of pus evacuated. Abscess reformed and opened again. Finally involved the cheek, with characteristic reddish-purple color.

Treatment. Infected area curetted. Teeth extracted. Potassium iodide internally.

Result. Cured.

Remarks. No recurrence.

CASE 12.—Wife of farmer, aged thirty years, residing at Ontario. Seat of disease, jaw and cheek. Duration of symptoms before admission, three months. Admitted, November, 1904.

Chief Features of Illness. Small swelling opposite left lower wisdom tooth. Varied in size. Tooth extracted. Disappeared but reappeared shortly afterward. Cheek became involved. Skin over central part had the characteristic color.

Treatment. Teeth extracted. Mass excised.

Result. Cured.

Remarks. No recurrence.

CASE 13.—Plumber, male, aged fifty-four years, residing at Montreal. Seat of disease, jaw and cheek. Duration of symptoms before admission, three months. Admitted, January, 1912.

Chief Features of Illness. Last left lower molar extracted. Face became very much swollen just below angle of jaw. Incision into mass; found very firm with cartilaginous appearance. Little bleeding and small amount of serosanguinous pus and granules. Over one softened area there was the characteristic purplish color of skin.

Treatment. Incision. Packed with iodoform gauze. Potassium iodide.

Result. No improvement.

Remarks. This is a recent case, and has not had time for any definite development.

CASE 14.—Thresher, male, aged twenty-four years, residing at Montreal. Seat of disease, cervical glands. Duration of symptoms before admission, two months. Admitted, December, 1911.

Chief Features of Illness. Small, hard lump appeared on right side of neck in front of the sternomastoid below angle of the jaw. Firm, not painful. Increased gradually in size. Gives history of chewing straws. Teeth in lower jaw all decayed.

Treatment. Several operations. Incisions. Gauze packing. Washing with weak solution of iodine. Potassium iodide internally.

Result. No improvement.

Remarks. A recent case; not long enough time to give result. Was not diagnosticated for some time. Small amount of sero-sanguinous pus.

CASE 15.—Clerk, male, aged twenty years, residing at Montreal. Seat of disease, cheek. Duration of symptoms before admission, two months. Admitted, April, 1908.

Chief Features of Illness. Small abscess appeared near lower right molar teeth, which were not in good condition. Mass lanced by dentist; small amount of pus escaped. Condition did not improve. Finally cheek involved. Central part softened and skin over it had a peculiar dusky red color.

Treatment. Opened. Cured. Packed with gauze. Teeth extracted. Potassium iodide internally.

Result. Cured.

Remarks. After-history not obtainable.

CASE 16.—Female, aged nineteen years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, one month. Admitted, December, 1905.

Chief Features of Illness. Toothache in upper left molars. Teeth had been treated previously. Gum-boil appeared. Lanced by dentist; disappeared, leaving an indurated mass. Injured cheek in this area and became immediately swollen. On entrance to the hospital central part of swelling was soft, with characteristic color. Evidence of fluctuation.

Treatment. Teeth extracted. On roots of molars small abscess sacs were noted. Excision of cheek tissue. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Injury here seemed to light up the process.

CASE 17.—Grain merchant, male, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, two months. Admitted, December, 1905.

Chief Features of Illness. Mass appeared in gum near bad teeth which were removed. Incision by dentist. Small amount of blood-stained pus escaped. On entrance to the hospital skin of the cheek was slightly involved.

Treatment. Cured. Packed with gauze on two occasions. Potassium iodide internally.

Result. Cured.

Remarks. No recurrence.

CASE 18.—Male, aged forty-two years. Seat of disease, cheek. Duration of symptoms before admission, two months. Admitted, December, 1905.

Chief Features of Illness. A small mass appeared in left cheek, the size of a bean, gradually increasing in size, and becoming soft, dark purplish-red in color. On incision a small quantity of blood-stained purulent material escaped, leaving a discharging sinus.

Treatment. Excision. Potassium iodide internally.

Result. Cured.

Remarks. Sent to the hospital as tuberculosis. (Usually no diagnosis sent with these cases.)

CASE 19.—One case in O. D. department. Incised, packed with gauze, but patient never returned for further treatment.

GROIN CASES.

CASE 1.—Wife of farmer, aged twenty-nine years, residing at Ontario. Seat of disease, left groin. Duration of symptoms before admission, two months. Admitted, March, 1903.

Chief Features of Illness. Pain in lower left quadrant, with frequency of micturition. Two weeks ago mass appeared in groin above Poupart's ligament. History of diarrhea for some time past. Urine normal.

Treatment. Incision; packed with iodoform gauze. Potassium iodide internally. Discharged.

Result. Cured.

Remarks. Never established any relationship with bladder. Two years later a small abscess developed near scar, which was opened by her doctor, curetted, and potassium iodide given internally. Since then she has been perfectly well.

CASE 2.—Housework, female, aged forty-eight years, residing at Montreal. Seat of disease, left groin. Duration of symptoms before admission, two months. Admitted, January, 1908.

Chief Features of Illness. Complained of weakness and loss of weight. Five weeks ago noticed pain in left lower quadrant which lately had been very severe. Twelve days ago a small mass appeared in left groin, the centre of which is soft while the periphery is firm and hard and infiltrates the abdominal wall. Bowels constipated.

Treatment. Incision. Small quantity of foul-smelling pus escaped. Packed with gauze. Drainage. Potassium iodide internally. Discharged.

Result. Cured.

Remarks. Apparently entirely in abdominal wall. Foul odor due to colon infection. (No mention of hemorrhoids or other lesions about the rectum or the anus in this case.)

CASE 3.—Cheesemaker, male, aged twenty years, residing at Province of Quebec. Seat of disease, left groin. Duration of symptoms before admission, six months. Admitted, August.

Chief Features of Illness. Began with pain of dull aching character in epigastrium, which later localized to left lower quadrant. Pain became very severe, and mass appeared just above Poupart's ligament. Patient walked with limp.

Treatment. Incision. Evacuated blood-stained seropus containing numerous granules. Packed with iodoform gauze. Potassium iodide internally.

Result. Improved.

Remarks. Left the hospital with sinus. Later information could not be obtained. (No mention of hemorrhoids or lesions about the rectum or the anus in this case.)

SKIN CASE.

CASE 1.—Laborer, male, aged thirty-six years. Seat of disease, skin. Duration of symptoms before admission, one year. Admitted, September, 1905.

Chief Features of Illness. Began as small callous spot at inner part of thenar eminence of right hand; about the size of a split pea when first noticed. Cracked and exuded a small quantity of blood-stained serum. Finally a definite ulcer formed which was cauterized and excised. Small ulcer returned in scar, beginning as small vesicle outside of which more vesicles occurred; gradually coalesced, forming large ulcer; base, dark red covered with sloughy material. Skin in neighborhood dark blue color.

Treatment. Excised. Potassium iodide internally.

Result. Cured.

Remarks. Organism never isolated.

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HEMA-URO-CHROME:

A NEW LABORATORY TEST FOR CANCER AND SARCOMA, ALSO A METHOD OF SEPARATING BILE ACIDS AND PIGMENT WITH THE APPLICATION OF TORQUAY'S TEST, INDICAN BEING OBTAINED IF PRESENT. A PRELIMINARY REPORT.

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URINE, being a secretory excretion, has from time immemorial been subjected to more or less inspection and examination, as affording clues to pathologic conditions in various tissues and organs of the body. As is usual in all progressive studies, while the substances found have remained the same, the interpretation has changed with increased knowledge. Albumin in the urine does not signify Bright's disease; indeed, I doubt if many physicians of today have read Bright's classic. It is not a common disease of the kidney, and in many text-books the description is greatly confused. Neither do the albumoses, or Bence-Jones body, signify chronic suppuration or disease of the bone-marrow, for they are found in many diseased conditions, especially in those of malignant or "near malignant" character. Many tests for bile in the urine have been proposed, and during years of experience in the examination of urine I have had opportunity to try them all. Most have been unsatisfactory and uncertain, even when the bile acids and coloring has been obtained in a concentrated form by the following method (which is, so far as I am aware, original).

To 100 c.c. urine in a flask of about 150 c.c. capacity add 10 c.c. hydrochloric acid; heat over a slow fire until ebullition begins. Remove from the fire and when cool add 30 c.c. ether. Agitate occasionally by turning the flask, avoiding hard shaking, which interferes with removal of the ether. After about twelve hours remove the ether into a clean white dish; allow it to evaporate spontaneously, when the bile acids and coloring matter will be left upon the bottom of the dish. The bile acids may be converted into salts by the addition of a small amount of a 1 per cent. solution

of sodium acid-carbonate (bicarbonate) in water and the several tests applied.

Some four years ago my attention was attracted to Torquay's test, which is a recently prepared solution of methyl violet, 1 to 2000 of water. (Practically one drop of the saturated alcoholic solution in an ounce of water.) Two tubes of equal size are partly filled with this solution; to one is added a small amount of the above solution of bile, which discharges the blue tint leaving the red. Comparison of the tubes renders the color change very distinct. Indeed, it is the most distinctive test for bile I have used. Having verified its reliability, which has also been done by a German observer, using the several substances obtained from urine, I can commend it.

Indican if present will be seen on the white dish as a ring above the bile acids and coloring. After chloroform or ether anesthesia, acicular crystals of ammonium chloride will be deposited and in some pathologic conditions cystin and fatty substances found. During the use of this method I would occasionally find the ether pink, even red in color and upon evaporation a more or less heavy deposit of hematin would be seen above the indican and constituents of bile.

Observations extending over more than four years lead me to state that this pink coloration may occur to a slight degree in diseased conditions of the liver when the hepatic cells are unable to convert the product of the lysis of erythrocytes into bile acids and coloring substances; therefore it occurs in cholemia from any cause and in jaundice, especially the hematogenous form. It will be found when the urine contains red blood cells from any cause, whether acute nephritis or hemorrhage, from some portion of the urinary tract. These may be differentiated by the microscope and removed before further testing. The pink tint appears due to a cleavage product of hemoglobin, probably hematin, and is present in larger amounts in the several infectious fevers, malaria in all its forms, greater in the severe types, as in the "tick-fevers" of Central America and Mexico, in babesia, piroplasmosis, etc. In the urine of a woman from Yuma, Arizona, with anemia, the hemoglobin content being only 35 per cent., in whose blood a spirillum staining blue with Giemsa was found, the hematin was strongly positive.

Hematin will be present in the urine of the anemias associated with tapeworm, uncinariasis or hook-worm, and other intestinal parasites. It will be present in greater amount in the anemias due to disease of the blood-making organs, and in the essential anemias due to near malignant disease of the lymph and ductless glands, especially in hyperthyroidism and in splenic, myelogenous, and pernicious anemia, the hematin being in proportion to the destruction of erythrocytes. While the tint and depth of color

will vary with the proportions of bile, indican, hematin, and urochrome present, by far the greatest amount and intensity of color obtained by the process described was found in the urine of patients suffering from malignant disease, cancer and sarcoma. *I have never found it absent in cases of cancer or sarcoma even when of small size or unsuspected.*

So far as possible all the cases hereafter mentioned have been subjected to the pathologic test, after clinical, surgical, and laboratory examinations, that the statements made might be verified.

The urine of these patients does not differ macroscopically from normal urine; it is not smoky as is urine containing blood, nor reddened, as in hemoglobinuria.

By the process described, a deep red urochrome is liberated by the action of hydrochloric acid and heat and taken up by the ether.

Chemical and spectroscopic examinations indicate that it is derived at least in part from the red-blood cell, but there is in the urine of patients suffering from cancer and sarcoma a substance other than hematin; but as the chemistry of the urochromes is so involved and contradictory, I hesitate to affirm its composition.

It appears from the evidence obtained to belong to the tryptophan, pyrrol or indol group, possibly indoxyl red, hence we may regard this red urochrome as a mixture or combination of hematin and an indoxyl base, produced by the lysis of erythrocytes and the destruction of proteid by the cancer cell. That we might have a convenient term by which to express this substance and indicate its source, I have chosen tentatively the compound word, "hema-uro-chrome."

I have examined the urine from a number of cases of malignant growth not enumerated and have made control examinations of blood and urine almost innumerable during the past four and a half years. To indicate the variety of cases examined and the assistance rendered by friends I will cite the following: More than four years ago, being convinced of the presence of this hema-uro-chrome in the urine of cancer cases, I asked Dr. W. H. Dukeman, for a specimen of urine from a patient with cancer of the rectum, and found it strongly positive. Portions of the growth were examined by me and by Dr. C. C. Warden, pathologist, who confirmed the diagnosis of rectal cancer. Dr. Dukeman later brought a catheterized specimen of the urine from a case of continuous uterine hemorrhage, due to a suspected cancer of the uterine body. The hema-uro-chrome test being strongly positive, I concurred that a hysterectomy was indicated, the diagnosis being confirmed by the same pathologist. About three years ago Dr. Dukeman brought the urine from a patient suffering with sarcoma of the neck, which after examination, he pronounced inoperable. The patient went to Dr. W. A. Mayo, of Rochester, Minnesota, who after a surgical and pathologic examination declined to operate; in this case the

hema-uro-chrome test was markedly positive. It was strongly positive in sarcoma of the eyeball under the care of Dr. F. E. Detling. In a small epithelioma of the eyelid and in two cancers of the pharynx under the care of Dr. H. A. Kiefer, the relative quantity was surprisingly great. In cancer of the tongue the tumor being removed by Dr. Granville MacGowan, the test was positive and traces remained in the urine for more than three months, gradually disappearing. This growth was *very small* and Dr. Stanley P. Black, who made the pathological examination, stated, "It was in the very beginning difficult to find and determine the true nature." Dr. Black had opportunity to apply the test where, after removal of a breast for cancer, recurrence with metastasis to bone and omentum occurred, confirmed by autopsy. Here the hema-uro-chrome was present in large amount. I have advised operation for mammary cancer when the growth was so small the surgeon hesitated to operate, upon a positive finding of the hema-uro-chrome, being justified later by the pathologist. I have had urine from many cases of cancer of the face, lip, and jaw of small and large size through Drs. Edwards, MacGowan, Crum, Stoner and others, all of which were positive. Through the kindness of Dr. Shippey, of the Soldiers' Home, and Dr. M. G. Gates, from the County Hospital, I have had many specimens with extensive involvement, metastasis, or general carcinomatosis; the amount of the hema-uro-chrome bore a distinct relation to the extent of the cancer process. I had opportunity to apply the test with positive results in cancer of the thyroid, causing necrosis of the tracheal cartilages and death, through the courtesy of Dr. Sutton, of Zanesville, Ohio. Through the courtesy of Drs. MacGowan, Dillingham, Hart, and others several specimens of urine, where cancer of the bladder was under consideration, gave negative results, confirmed by cystoscopy or operation. Also, two cases of cancer of the sigmoid were strongly positive, as was an unsuspected cancer of the transverse colon.

Two cases difficult of diagnosis, cancer being under consideration, in the practice of Dr. William A. Edwards, one being a pathological condition affecting the transverse colon, the other the stomach, gave negative results as to the hema-uro-chrome, but strongly positive reactions for bile by Torquay's test; which suggested the possible elimination of cancer by the test, thereby extending its application. Dr. A. F. Zimmerman had under his care a man presenting the symptoms of pyloro-duodenal cancer, the urine being negative as to hema-uro-chrome, but strongly positive to Torquay's test, with a large yield of bile-acids and pigment. I suggested a differential diagnosis of duodenal ulcer near the papilla, causing obstruction with resorption of bile. These cases indicate that the test may be used as a means of differential diagnosis. It presents to us three substances of pathological importance: bile, indican, and the hema-uro-chrome, each having a distinct significance.

I am not aware of the previous application of the uro-chromes in the diagnosis of disease. That the greater number of them represent pathiologic metabolism, especially when in excess, there can be little doubt.

It has long been known that cancer cells produce ferments or enzymes which cause hemolysis, cytolysis, and proteolysis. It is upon this fact that all serodiagnostic methods are based; hence the method I propose has a foundation similar to the methods of Salomon-Saxl and Salkowski, as well as the meiostagmin reaction. None are absolutely specific for cancer, but are suggestive, and will sustain a wavering diagnosis, being positive in at least 85 per cent. of cancer cases and present in only 15 per cent. of other diseases.

The method proposed by me is more simple, easy of execution, and less liable to error than any of the others, and other diseased conditions yielding hematin can be eliminated by methods known to all. That they may be compared, I have epitomized the best of these methods recently proposed.

Salkowski put forward colloidal nitrogen when found in the urine in excess of normal (3.42 per cent.) as diagnostic of cancer, and many careful observers since have agreed that colloidal nitrogen of 6 to 7 per cent. is positively diagnostic of cancer.

Mancini, however, calls attention to the fact that colloidal nitrogen passes into the circulation and is eliminated by the kidneys in larger proportion than normal in many morbid conditions. He found this to occur in pulmonary tuberculosis, in many suppurative processes, in pleurisy, and in cirrhosis of the liver when the exudate is being absorbed, but not in so large a proportion as in cancer.

Caforio corroborates this statement, and states that the excess of colloidal nitrogen gradually disappears after excision of the cancer. The method of estimating colloidal nitrogen is as follows: If the urine is alkaline it is rendered slightly acid with acetic acid. If it contains albumin this is removed by boiling. After filtration the total nitrogen in 5 c.c. of the twenty-four hour urine is determined by Kjeldahl's method. One hundred c.c. of the same specimen is evaporated upon a water-bath to 10 c.c. cooled, and 100 c.c. of absolute alcohol added to precipitate the colloidal nitrogen. After standing several hours it is thrown upon a filter and the precipitate washed with alcohol until all traces of urea are removed. The precipitate is then dissolved in hot water and the nitrogen determined by Kjeldahl's method, from which the colloidal nitrogen can be determined.

Salomon and Saxl found increase of the sulphur-containing oxyproteids in the urine of more than 70 per cent. of cancer cases, even in those well nourished; while in 150 control cases they found only one which showed such increase, and that in a moribund case

of cirrhosis of the liver. After removal of the sulphates by barium chloride they propose to oxidize the neutral sulphur-containing oxyproteids by hydrogen peroxide then to estimate the sulphates, in this manner determining the sulphur oxyproteids.

Breiger's antitrypsin test is not specific, but negative findings appear to exclude cancer.

Among recent reactions of the stomach contents, Salomon's test has proved valuable, frequently disclosing an unsuspected ulcerating gastric cancer, although a benign ulcer may occasionally give the reaction. The technique is as follows: For a day before the test is to be made the patient does not eat anything containing albumin and restricts himself to fluids. In the evening the stomach is washed out with 400 c.c. of decinormal salt solution, and again in the morning with the same amount. The latter is tested for albumin by Esbach's method and for nitrogen by Kjeldahl's method. If positive to Esbach's and 20 mg. of nitrogen are found by Kjeldahl's it is evident an ulcerating cancer is present, although a benign ulcer has given the reaction.

Salomon and Falk's salicylate test is one of the latest contributions to the diagnosis of gastric cancer. The stomach of the fasting patient is washed out, after which a rectal enema containing 3 gm. sodium salicylate is given. As soon as salicylic acid can be detected in the urine the stomach is washed out and the rinsings tested for salicylic acid. While salicylic acid cannot be detected in the rinsings from a healthy stomach, and rarely in those from one with benign ulceration, it is found in the rinsings from an ulcerating cancer.

The glycytryptophan test is liable to error, because of regurgitation of the duodenal contents as well as the presence in the saliva of a peptidolytic enzyme.

According to Freund and others the meiostagmin reaction is simple and reliable. In this, advantage is taken of the cancer cells' destroying power of normal blood serum; but difficulty is often experienced in obtaining suitable cancer-cell material, for in many cases cancer cells are not destroyed by serum. The basis of the reaction is the fact that when the antibodies of a disease and the corresponding antigens are brought together there is a lowering of surface tension in the mixture, with a change in the rate of dropping of the fluid from the stalagmometer, as the special pipet is called.

Izar has lately reported upon a meiostagmin inoculation reaction, the findings of which were positive when the original meiostagmin reaction failed. He found that an aqueous emulsion of an ether or methyl-alcohol extract of malignant tumors heated to 50° C. (122° F.) acquired extremely toxic properties. When a mixture of such an extract and blood serum is centrifuged the toxic properties are concentrated in the supernatant fluid in the non-

malignant cases, while in sarcoma or cancer it remains in the sediment. Furthermore, this sediment suspended in salt solution and injected into rabbits caused their death in twenty-four hours. This he calls the "meiostagmin reaction *in vivo*."

This brief review of recent work in the diagnosis of cancer will emphasize the simplicity of the test I propose.

It has long been recognized that any treatment of cancer, to be successful, must be instituted early in its existence, the earlier the better. It is for this reason that many have endeavored to find a laboratory test which would give assurance that a suspicious tumor growth was malignant, and its removal justifiable without cutting into it, that a portion might be obtained for microscopic examination.

Bergel calls our attention to the fact that early in the existence of a sarcoma or cancer tumor it is surrounded by a zone of inflammation, as is any foreign body, this being the natural attempt of the organism to protect itself. So long as this barrier is unbroken the cancer cells are not disseminated; but when this protecting wall is broken by feebleness of cell resistance or by traumatism, extension by contiguity or by metastasis will occur. He calls attention to the fact that horse serum has a tendency to deter the growth of cancer cells.

Investigating the use of serum, he found that fibrin was the only constituent which gave rise to a typical aseptic inflammation, with great leukocytosis, serous or fibrinous exudation, with fibroblasts and the formation of new connective tissue without producing anaphylaxis or other ill effects. He found that injections of pure fibrin (in the form of Merck's substitol, 5 grains of which are equal to two and a half fluidounces of serum) not only inhibited the growth of the cancer but caused a definite shrinkage of the tumor. The substitol was suspended in salt solution.

More recently Wassermann, working with Keyser and M. Wassermann upon "mouse cancer," found an eosin-selenium compound, which has the power of causing softening, disintegration, and absorption of such malignant tumor. Wassermann found that eleven daily injections of this eosin-sodium-selenium compound into the caudal vein of white mice caused the disappearance of the tumor without recurrence, but earlier interruption of the treatment was followed by recurrence of growth. If the tumor was not larger than a hazelnut no untoward effects occurred, but the softening and absorption of a large growth could but of necessity produce untoward effects not only from the selenium or tellurium, but from the hemolyzed tumor products. Wassermann cautions us that "this product has not as yet been applied to man," neither has the mode of preparation or its composition been made public. However, its successful use in "mouse cancer and sarcoma" without recurrence justifies the hope that some

similar substance may be found and applied to the treatment of malignant disease in human beings. Such treatment must of necessity be instituted early in its existence. This depends upon an early diagnosis.

No certainty exists as to the origin of these neoplasms, the ignorance upon the question being almost appalling. The fact that I have never failed to find this hema-uro-chrome present in cancer furnishes my excuse for presenting this preliminary report.

Wassermann's treatment is based upon the following facts: Heliotropism of cells and collections of cells constituting vegetable and animal life has long been recognized and the chemical activity of the more refrangible rays from blue to the ultra-violet is well-known to be greater than the yellow and red rays, a fact utilized in the various "light treatments." It is but reasonable to suppose that the red rays lessen the activity of nuclear division or mitosis and have a tendency to produce a more resistant cell, a condition observed after the use of Ponceau, also known as Schâarlach and Beibrich's red. It was observed by Wassermann, working with Ehrlich, several years ago, upon "dye stuffs," that cells derived from the epiblast had a strong chromo-chemo-taxis for dyes of the fluorescein group, especially for eosin, which led him to employ eosin as a carrier for the cell-destroying selenium and tellurium. He bases his use of selenium and tellurium upon the findings of Gosio, who about four years ago found selenium and tellurium, or their salts, a reliable method of differentiating degenerating and dead cancer cells from living cells, an almost black precipitate being deposited about the nucleus of degenerating or dead cells. Both Gosio and Wassermann are apparently ignorant of the fact that homeopathic experimenters or observers called "provers," more than thirty years ago, found that selenium and tellurium as well as their salts have selective affinity for cells derived from the epiblast. Selenium affects them less than the more powerful tellurium, which causes degeneration and death of epidermal cells as well as of nerve endings in the deeper layers of the skin, affecting even the spinal nerves, extending from the seventh cervical to the fifth dorsal. It may be recalled that these supply practically all the muscles of respiration, including accessory muscles. Large doses cause death by asphyxia; for the authenticity of which I refer to Richard Hughes.¹

Selenium and tellurium are non-metallic elements of the sulphur group. They form oxides, acids, and salts similar to sulphur, but appear to have a more destructive effect upon cells derived from the epiblast, especially if irregular or atypical. The success of Wassermann's work upon mouse cancer gives hope that a similar substance may be found of service to man, but to be of service it

¹ Manual of Pharmacodynamics, 1886, 5th ed., p. 803.

must of necessity be used early in the development of the tumor or malignant growth. Hence an early diagnosis is imperative. For that reason I present this test, with some of the evidence, trusting it may be of service. It is easily applied and based upon a sound foundation, viz., the passing into the circulation and elimination with the urine (a natural excretion) of the products of hemolysis, cytolysis, and proteolysis by the cancer cell during its growth and extension.

In cancer the amount of the hema-uro-chrome must of necessity vary with the activity and extent of the cancer process, and I do not believe a percentage proportion would be of value if determined. I have therefore depended upon the relative amount of the hema-uro-chrome obtained from a definite quantity of urine by a certain amount of hydrochloric acid and ether.

I hope that which I have presented will aid in the diagnosis of cancer at a period when removal by operation or some form of medication may rid the individual of a terrible menace.

Beside, a negative finding will enable us to relieve that mental distress associated with a suspicion of cancer or of its recurrence.

A PSYCHOSIS FOLLOWING CARBON-MONOXIDE POISONING, WITH COMPLETE RECOVERY.¹

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AMONG the various toxic psychoses which have come under my observation in the Government Hospital for the Insane, one which was produced by carbon-monoxide poisoning is of special interest, in view of the fact that the patient suffered from a severe intoxication which resulted in the development of mental symptoms one month following the accident, and terminated in a complete recovery. That psychic disorder is one of the sequels of this form of poisoning has long been recognized, yet few cases have been recorded in this country. A careful review of the literature yields scanty information as to the clinical and pathological course of this toxemia, notwithstanding many accidents occur in our large cities and collieries. However, some valuable observations on this subject can be obtained from foreign publications.

Cases of carbon-monoxide poisoning may be accidental, suicidal, or homicidal, or the latter two may be combined. In France four-fifths of the suicides are caused by poisoning with carbon-

¹ Read at the International Congress on Hygiene and Demography, 1912.

monoxide gas. In the large cities of this country scarcely a day passes without a number of cases are recorded of accidental or suicidal intoxication from this gas. According to the daily papers in New York City alone there were reported to the coroner in the first six weeks of the present year seventy-five fatalities. Deaths by gas poisoning have been steadily increasing for the past twenty-five years, and this increase has been due to the manufacture of illuminating gas by a method known as "water gas." This gas has come to be such a serious cause of death, that a point has been reached where it behooves the health authorities and others interested in the subject to consider what steps can be taken to curtail this mortality. However, at present there are no available statistics of these accidents or fatalities. The last "Bulletin of the United States Census Bureau on Mortality Statistics" does not group these deaths independently, but includes them under the general head of Mortality from Intoxication. In 1910 the Bureau of Commerce and Labor issued a Bulletin on "Fatal Accidents in Coal Mines." This report furnishes no information concerning the effects of such intoxication upon those who escaped death.

In recent years many of the States have appointed commissions to investigate occupational diseases, and in 1909 these commissions united as a permanent organization known as the National Conference upon Compensation for Industrial Accidents, with the object in view to obtain uniform legislation for men engaged in dangerous occupations. In connection with this the International Association for Labor Legislation has prepared a plan for the protection of workmen exposed to the dangers of industrial poisons in order that they may be able to get adequate legislation regulating the same. A committee of this society has compiled a list of these industrial poisons, and recently the United States Department of Commerce and Labor has published the following tabulated list, which deals with the source, chemical and physical properties, and the industries in which the poisoning occurs, together with the toxic symptoms following exposure:

"Carbon monoxide is described as a colorless, tasteless gas, and when in a state of diffusion is odorless, burning with a blue flame in the air. Coal vapor has about 0.5 per cent. of carbon monoxide. Illuminating gas, 6 to 10 per cent. carbon monoxide and 33 to 40 per cent. of mine gas. Water gas, a mixture of 41 per cent. carbon monoxide, 50 per cent. hydrogen, 4 per cent. carbon monoxide, 2 and 5 per cent. nitrogen. Producer gas contains 34 per cent. carbon monoxide and 60 per cent. hydrogen gas.

"Branches of industry in which poisoning occurs: In industrial plants with defectively planned or ill-tended firing and heating arrangements; plants for the production of industrial gas; mining (mine gases); coal mines; blast furnaces (furnace gas); Cowper apparatus; gas purification; coke ovens; smelting furnaces; gas

machines; lime and brick kilns; dolomite calcining kilns; iron and metal foundries (drying of the molds); soldering in tin shops; charcoal burning; resin distillation; ironing; heating with open coal brasiers or coke stoves (drying the plaster and walls of new buildings); drying chambers."

Another source of danger from this gas has arisen in recent years from the extensive use of benzine and gasoline explosive engines, which are installed in the motor car, motor boat, and aeroplane. Investigations following accidental death from the gas escaping from such engines revealed the fact that the men attending the engines in the cabins of launches often have toxic symptoms—headache, dizziness, etc. In this connection it is the opinion of Surgeon-General Stokes, of the United States Navy, that noxious gases generated by exploded powder in the turrets, from burning coal in the fire rooms, and other gases similar to carbon monoxide in illuminating gas, are responsible for the collapse and sometimes death of men working in the above spaces.

To quote further from the Bulletin, the symptoms of acute poisoning are: "Increased blood pressure at first, with slowing of the pulse and pounding heart beat; later, lowering of the pressure, with rapid but small pulse, and, not infrequently, with discrete spots of dilatation in the superficial bloodvessels. Remarkably pale red discoloration of the blood and of the dilated spots; formation of carbon-monoxide hemoglobin is demonstrable by the spectrum. (a) Disturbances of the general health. In mild cases, dull headache; flashes before the eyes; giddiness; ringing in the ears; nausea and fulness in the gastric region. (b) In severe cases: Bluish discoloration of the skin; spasmodic, wheezing respiration; sometimes tonic and clonic convulsions; more often paralytic symptoms, either with weakness of all the extremities, or the lower only, or indeed of only single groups of muscles, including also the facial muscles. The convulsive stage, which may be altogether absent, is succeeded by the stage of asphyxia, with sensory and motor disturbances, involuntary voiding of urine, semen, and feces; subnormal temperature; weak, slow, and intermittent pulse; loss of consciousness. As sequels there have been observed pneumonias, inflammations of the skin, paralyzes and psychoses, the last two often pursuing an unfavorable course. Chronic poisoning (among ironers, firemen, cooks, etc.): Frequent headaches; dizziness; nausea; vomiting; coated tongue; weakness of memory; anemia without chlorosis; "hot flushes;" formication; palpitation of the heart; insomnia; general debility and feebleness of the psychic functions."

Ziehen describes the chronic monoxide poisoning which affects those employed in laundries as ironers, firemen, and others who work in crowded, overheated places in which there are bad heating arrangements, and in which these people are obliged to remain

for some considerable time. It manifests itself in general nutritional disturbances, and presents a picture of mental and bodily fatigue which is sometimes regarded as either neurasthenia or hysteria.

The following is the clinical record of the case:

CASE No. 18,888.—M. A. O., aged forty-five years; native of Ireland; single; indigent; admitted December 10, 1910.

The following history was supplied by an aunt of the patient, with whom she made her home. After the patient's return to her normal mental state she corroborated this information.

Family History: Negative so far as could be learned as to nervous or mental diseases, epilepsy, etc.; mother died of tuberculosis at the age of thirty years.

Personal History: Born in Ireland; was elder of two children; always healthy; common-school education. After her mother's death kept house for her father until she came to this country, at the age of twenty-eight years. Upon her arrival in this country she obtained employment as a domestic, and was evidently an efficient servant, as she was employed for a number of years by prominent families in this city, including those of a United States Senator and a German Ambassador. She was of a cheerful disposition, habits good, and always attended to her religious duties. Was fond of reading history, fiction, periodicals, etc. On November 2, 1909, she went to bed in her usual good health, and the following morning was found in a deep coma. Upon investigation it was found that illuminating gas was escaping from a defective fixture in the room which she now occupied for the first time upon her return from her vacation, not knowing that the stop-cock was broken, though this fact was known by the other servants in the house. Had it not been for an open window the accident would probably have been fatal. She was at once removed to the George Washington University Hospital, where she remained in an unconscious condition for four days. The informant called on her four days after the occurrence, but at this time was unable to arouse her. However, on the sixth day the patient recognized her, although she was dull of comprehension and appeared somewhat somnolent. From this time on the patient daily improved, and was discharged November 13, 1910, having recovered from the acute effects of the poisoning.

Abstract of record from the George Washington University Hospital, where she was first taken immediately after the accident: Admitted to the George Washington University Hospital, November 3, 1910. For the first twenty-four hours patient's temperature fluctuated between 101° and 100°; pulse between 120 and 82; respirations 40 and 22. Was given oxygen on admission and normal salt solutions frequently, at least every four hours; hot applications externally. Patient began to perspire about three hours after

admission. She was given oxygen every hour for a short time. Hypodermoclysis of 500 c.c. was given.

Summary: At the end of first day: Nurses' notes: Was catheterized. Patient perspired a great deal. Hot bottles; oxygen every hour, for fifteen minutes during the last eighteen hours. Patient turned on her side for a half hour during the night.

Summary: At end of second day: Maximum temperature 101°, minimum 98.6; pulse 100 to 80; respirations 30 to 24. Oxygen given every hour, for fifteen minutes. Hot applications; normal salt injections. Nurses' observations: Patient restless all night; seemed more rational.

Summary: At end of third day: Maximum temperature 100°, minimum 99°; pulse 100 to 70; respiration 30 to 24. Oxygen given. Saline solution discontinued. Patient conscious at intervals; slept very little; complained of pain in back; very restless all night; slept at intervals.

Summary: At end of fourth day: Temperature normal; pulse 78° to 70°; respiration 26 to 24. Patient restless all night, complaining of pain in back and neck; slept about one hour. Patient tossed about the bed; got out of bed.

Summary: At end of fifth day: Maximum temperature 98.6° to 97.8°; pulse 80 to 78; respiration 28 to 24. Patient very quiet during the day; restless all night; complained of pain in back; asked to get out of bed. Slept from one o'clock on at intervals.

Summary: At end of sixth day: Temperature normal; pulse 80 to 74; respiration 24. Patient very restless all night; complained of pain in the back; wanted to get out of bed. Slept about three hours.

Summary: At end of seventh day: Temperature normal; pulse 80 to 74; respiration 24 to 22. Patient very restless all night; slept about four hours during night. Very nervous. Given regular diet; eats well. Voided urine.

Summary: At end of eighth day: Temperature normal; pulse 78 to 76; respiration 24 to 22. Patient very restless; slept about four hours during the night. Very nervous; given regular diet; eats well. Voided urine. Patient sat up in chair during the day.

Summary: At end of ninth day: Temperature normal; pulse 80; respiration 24. Patient up during the day; walked about; slept well.

November 13, 1910. Tenth day: discharged.

Upon her return to her aunt's home she continued to improve, and after two weeks was allowed to go back to the place where she had been working, as relatives and friends at this time considered her well. Soon after she resumed her duties the servants with whom she was associated noticed that she was becoming dull and forgetful about her work. She gradually became worse, and on

this account at the end of a week she was taken back to the home of her aunt, where she remained until her admission to this hospital.

While at her home, one week later, her aunt observed that her actions were peculiar; her movements were very awkward and her memory seemed to be a complete blank. She had outbursts of laughter without provocation; did a great many irrational acts; for instance one day she was noticed trying to put the trousers of a little boy on for a waist. She put her hands through the legs and tried to pull the trousers over her head. She was unable to find her way about the house. One day she wandered from her aunt's house to the United States Treasury Building, where she accosted a policeman and told him that she was in search of the house on U Street where she was formerly employed. She was directed to the residence and found her way there safely. A few hours afterward she was again taken back to her aunt's home. At this time she was oriented to person and place, but could not tell the hour, day, month, or year. Was unable to attend to her personal wants, became very untidy; would not remain in bed; and finally passed into a state of confusion and was brought to this hospital December 10, 1910, thirty-eight days after trauma.

On admission to this hospital, December 10, 1910, the patient was in a semistuporous condition; would answer questions promptly; was able to give her name, but all other replies were incorrect and irrational. She extended her tongue when told to do so, but otherwise was unable to carry out the simplest orders given her; was spoon-fed, as she was unable to feed herself. Throughout examination patient showed causeless laughter.

Physical Examination: Patient was in bed; well-nourished white woman; height five feet two and a half inches; weight 120 pounds; mask-like facial expression; hair dark brown mixed with gray, fine in texture; slight lateral scoliosis; deformity of sternum at articulation of the gladiolus with the manubrium; ears small; right antihelix more prominent than the left; complexion sallow; superfluous hair on face; skin free from eruptions; mucous membranes moist and pale; tongue coated, eroded on tip; gums inflamed; pyorrhea alveolaris marked; breath foul; appetite poor; bowels regular. Heart normal in outline; slight presystolic murmur over apex. Protruded tongue showed slight tremor; pupils equal, reacted promptly to light and accommodation; knee-jerks exaggerated, right greater than the left; plantars diminished; anesthetics over the whole surface of the body, including the face; she showed no reaction to deep pin-pricks, although to some extent this may have been due to the mental dulness. She could not recognize heat or cold when applied to the surface of the body, nor was she able to distinguish the gustatory tests used—salt, sour, sweet, or bitter; called a solution of quinine when placed on her tongue, sour; unable to recognize any of the olfactory tests; said pepper-

mint was bitter, cloves didn't know; called stench hartshorn; astereognosis present; grip, right hand 14 kgs.; left hand, $9\frac{1}{2}$ kgs.; coarse tremor of extended hands; gait unsteady and uncertain; balancing power impaired, involuntary evacuations of the bladder and bowels; urinalysis negative; no sugar, albumin, or casts.

Wassermann reaction with the blood serum and the cerebrospinal fluid negative. Cerebrospinal fluid clear; protein content not increased; Noguchi test negative. Cell count 1 per c.mm. Differential: lymphocytes, 98 per cent.; large mononuclears, 2 per cent.

The notes made for the next three days showed that mentally the patient was dull and apathetic; responded promptly to all questions, but was able to give little additional information in regard to personal matters; gave name of the country in which she was born, but could not give the name of the county or parish. Her replies were irrelevant and accompanied by outbursts of laughter. This tendency to laughter was also shown when she heard the voices of anyone around her or whenever anyone approached the bed. She had a mistaken identity of all persons in her environment, although she recognized her aunt on her visits. She appeared clearer so far as she was able to comprehend and carry out some simple orders given, although there was a retardation and some incoördination in all her movements. When asked where she was she said she was at home, but that she had just been down the river on a boat with President Taft and his daughter Helen. At this time she carried out the following orders after considerable hesitation: right forefinger on left ear; right hand on left knee; left hand on right knee.

The neurologic symptoms above mentioned still continued; deep reflexes all exaggerated. At this time there was present on both sides a wrist clonus, also a slight Babinski; anesthetics were still present, but there was an area on the inner side of the right thigh, just above the knee, about the size of a silver dollar, which showed a delayed reaction to pin-pricks.

The following is an abstract of the clinical notes for the next ten days, December 15 to 25:

Consciousness still clouded. She gave prompt replies to all questions, but still showed a tendency to confabulate; on one occasion said she had just returned from the Bureau of Engraving and Printing; that she was employed there, and again that she had been at her home. As a rule all replies were incorrect. Said she was born in Ireland, but when asked the county said first County Limerick and then County Mayo, when in fact she was born in County Clare. Still had a mistaken identity of persons, and showed uncontrollable laughter. Whenever she heard anyone speaking near her she laughed heartily without cause. She continued to have incontinence of urine and feces. At this time she was able to

comprehend and carry out simple orders as follows: Right forefinger on left ear; right heel on left knee; left heel on right knee; all movements were unsteady and ataxic. Romberg present; gait unsteady; marked Babinski. All deep reflexes were still exaggerated; there was marked clonus of both wrists and ankles on both sides. Anesthesias were not so marked; she was able to recognize deep pin-pricks on almost all parts of the body, but could not localize light pin-pricks.

During the next five days the patient showed some improvement. She had learned the names of two physicians, the head nurse, and two noisy patients in the ward, but was unable to identify them. She was disoriented to place and time. She was at this time able to give the names of one or two of her employers, the name of the church she attended in the city, the correct county and parish in Ireland in which she was born, and gave correctly the names of her relatives in this city and in Ireland. Falsification of memory continued: Said she was at the Y. M. C. A., and had just returned from the city.

The deep reflexes continued exaggerated; ankle clonus and wrist clonus present; also Babinski; anesthesias were not so prominent as formerly; patient responded to light pin-pricks on face, hands, and inner side of her legs and thighs.

During the next five days, December 30 to January 5, patient continued to improve, especially on the physical side. She appeared to be able to comprehend all instructions without much effort on her part so that she was able to coöperate. When told to put her right forefinger on her left ear she put her right forefinger on the right ear. When asked if that was correct she said, "No, you said my left ear." She then placed her left forefinger on her left ear. When asked to extend her right hand she extended her left hand. When told to extend her right and left foot she did so correctly. After five minutes these orders were again repeated, and this time she failed in all. She still showed some impairment of the stereognostic sense; she recognized a number of objects placed in her hands, but failed in several others. The physical examination at this time showed soreness of the teeth and tongue, mild gingivitis. Patient was hyperalgesic to pin-pricks of the face and ears, the nipples, sacral region, and soles of the feet. After much experimenting she recognized light touches of cotton wisps. Thermic sense appeared normal over the entire body; gustatory sense normal; olfactory: said camphor was smelling salt; stench, pleasant. Equality of grip, 10 kgs. each. Reflexes: triceps and radials and ulnars markedly exaggerated. Knee-kick exaggerated, with slight clonus; plantar and tendo Achillis present; no defense reaction from the feet; jaw-jerk present; abdominal absent; Babinski on both sides; slight Romberg present; gait ataxic; eyelids on closure and extended hands showed tremor; tongue deviated to the right

side. Five days later this patient was up and dressed; was able to feed herself and had sphincter control; said she was living in the Capitol Building; that she had been living there five years; said she was not insane, but had a weakened mind from taking gas.

For the next ten days, up to January 20, patient improved both physically and mentally; showed orientation, but was unable to recall any of the occurrences in her life for the past two months; assisted with work about the wards. She could recall all the principal events of her own life up to the time of the accident, but showed an anterograde amnesia for subsequent occurrences.

From this time on the patient improved rapidly; regained insight and reacted normally to her environment. A mental examination at this time, about February 1, showed that she had recovered her mental faculties, but there was an anterograde amnesia covering a period of three months.

As she was in poor physical health she was retained in the hospital until April 7, when she was discharged as recovered. The physical examination on that date showed the following results: Patient recognizes pin-pricks and light touches all over the body; thermic and stereognostic senses normal; olfactory and gustatory senses normal; no Romberg present; pupils respond sluggishly to light and accommodation; sympathetic scarcely visible; right and left triceps very active and exaggerated; radial and ulnar present; right knee-kick exaggerated; tendo Achillis diminished; plantar reflexes very slight; no defense reaction. Patient did very well in giving the above tests. She was willing to coöperate; her actions were inhibited.

If one seeks analogous cases of psychic disturbances from carbon-monoxide poisoning in the literature very few will be found. What strikes the attention most forcibly when the cases are compared with each other is that almost every case has its own stamp and each one presents a clinical picture different from the others. Le Dosseur has collected a number of cases in which the following mental disturbances followed: aphasia; acute delirium; transitory chronic delirium; mental confusion; amnesia; melancholia; dementia. On the physical side he found muscular paralyses of diverse types; hemiplegias; paraplegias and monoplegias; various trophic disorders; convulsions, etc.

The mental condition of this patient on first observation was deep confusion. She answered questions readily as one in advanced stages of senility is apt to do. All answers were accompanied by silly laughter and none were correct. However, the examination of the patient during the first few days showed that dementia was only apparent, and that there was a lack of power of attention and concentration which prevented intelligent conversation and made her replies unreliable and incorrect and the product of her own imagination.

The principal manifestation of psychic disturbance in these cases is a loss of memory. The amnesia produced by oxide of carbon poisoning is generally sudden in its appearance and not slow and progressive like traumatic or alcoholic amnesia; it is a characteristic symptom appearing suddenly and extinguishing at once the entire past, and reducing to almost nothing the perception of the present surroundings. It may be the only apparent symptom in a mild case of poisoning and soon disappears, or it may be accompanied with disturbances of attention. The amnesia may simulate the Korsakoff syndrome in the polyneuritic psychosis with confabulation, pseudo-reminiscences, etc. A defective memory may exist in a certain number of cases which recover. This amnesia is retrograde or anterograde in type; it is variable in course and intensity; in some cases it is transitory, lasting often only a few hours or days; in others it persists for months or years; or it may be continuous, and again it may require the use of memory exercises to produce any results. In this patient it lasted nearly three months, blotting out this period from her life. More than one month elapsed from the time of the accident until the mental symptoms developed, or at least were recognized, and her admission to the hospital. We are unable to determine from information received how much her memory was impaired after the acute effect of the poisoning had run its course. If there was a defect present it was not apparent to her friends and relatives with whom she came into daily contact. When she began to regain consciousness in the hospital she had a complete retrograde amnesia. After several weeks she showed anterograde amnesia only, that is from the time of the accident and subsequent thereto. The patient was able to recall the details of her life the day before the accident, but she could not recall any of the events occurring from the time she fell asleep in her surroundings on the evening of November 2 until the middle of the month of February, when under treatment in this hospital. After her recovery the total periods of amnesia were three months.

Sachs, who has compiled a treatise concerning these complications, says: "In the early stage of convalescence a total amnesia is especially typical, either extending over the time before the poisoning, retrograde, or to the things of the present, anterograde. The falsifications of memory which were noted in this case during the first month show the Korsakoff syndrome. Stierlin reports this symptom in two of his patients. In the records of these cases one finds the various forms of amnesia diversely associated. Le Dosseur cites Broudel's case of a physician, who following an incomplete intoxication, lost his memory totally. Arriving at his patient's house he forgot her name and the course of the illness in her case. The amnesia lasted eighteen months, at the end of which time he fully recovered. Le Dosseur mentions in his study

a lithographer who was amnesic to such a point that he was obliged to consult an indicating board in order to recall the colors that should be applied to each part of the plate. M. Bricard reports a case of a decided retrograde amnesia. A woman, aged twenty-one years, attempted suicide. The amnesia was complete in all that related to the suicide. She knows it because she was told of it, but doubted very much. As to events immediately preceding the suicide there was found a retrograde amnesia for at least one week.

Many writers call attention in this intoxication to a marked aphasia, although sometimes it is mentioned as a simple trouble of speech in the form of an embarrassment or stuttering. This apparently is not a true aphasia, but may rather be designated an amnesic aphasia, since with the disappearance of the amnesia the aphasia becomes less marked or disappears altogether.

Sometimes in coming out of the coma there appears an acute transitory delirium which may last a few hours, accompanied by excitement in which the patient is euphoric to a degree. This delirium is rarely accompanied by hallucinations, but in chronic intoxications the delirium is more prolonged, and is accompanied by various hallucinatory disturbances, which may take the form of delusions of persecution. At this stage our patient did not show delirious experiences of any description.

Kraepelin observed that when those affected first awake from the sleep of the poisoning in many instances there is an interval free from any disturbances which lasts days or weeks, and then suddenly or gradually the severe symptoms of the disease manifest themselves, and some relapses are recorded. In this connection Weidner says: "It is not possible to separate the after phenomena from the acute symptoms in a sharp manner, for in most cases the source of the same extends back to the acute stages with the exception of a few phenomena of special brain affections which appear after a free interval, or become manifest after such interval; and secondly, the boundary between the disturbances which must be ascribed to the acute poisoning and those which are to be understood as after phenomena are so labile that up to the present there appears to be no unity of opinion concerning them."

The case under discussion showed such a reaction to the effects of the intoxication, for after the acute symptoms had subsided she was well enough to be about her usual duties for at least ten days or two weeks before the mental symptoms became evident. Abrahamson cites a similar case in which a patient of his was comatose for two days following an acute intoxication from illuminating gas, when her intelligence returned and she went home. Two weeks later she developed a psychosis.

A marked reduction in the emotional field has been observed by many writers. Recently Pfeifer has described singular phenomena

which often attracts attention in poisoning from coal gas; that is, the fixed mask-like expression of the face. The emotional tone of this patient for nearly two months was one of indifference. There were abrupt outbursts of an irresistible tendency to laughter. These outbreaks were spasmodic in character, and occurred without provocation. All her replies were accompanied by causeless laughter and it was evident whenever anyone approached her bed. This emotion had no depth, as she laughed when a patient in the adjoining bed was weeping. In the intervals between these attacks of laughter her face was apathetic. This appears to be a common symptom in carbon-monoxide poisoning, and has been referred to by several observers. Some of these cases show changeable humors, for they rapidly change from despondency to laughter. Stierlin mentions lack of emotion in his study. One of his patients evinced this symptom, showing a lack of proper feeling toward his sweetheart, to whom he was engaged before the accident, and expected to marry shortly. To some extent this may be explained from the characteristic autopsy results which have been reported in a series of cases where the symmetrical centres of softening were in or about the vicinity of the optic thalamus, most frequently in the globus pallidus and the lenticular nucleus, and hence in those sections of the brain which are supposed to control mimicry.

A subnormal temperature is characteristic of the first stages of the poisoning, after which it rises rapidly, attaining the maximum the first twelve hours. No record of a subnormal temperature in this case was made. The first recorded temperature, 101° , was the maximum on the first day following the trauma. On the four subsequent days it fluctuated between this and normal, and from then remained stationary. Ravine cites a case of a high temperature being reported in a child, aged eight years, which reached 110° in eight hours, accompanied by a pulse rate of 120 per minute. The pulse rate of this patient was in relative proportion to the temperature.

On the physical side we found involuntary evacuation of the bowels and bladder, exaggerated tendon reflexes, with clonus, including the Babinski reflex. We also had disturbances of sensation, including anesthasias, hyperalgesias, etc. The involuntary evacuation of the bowels and bladder existed for about one month in this hospital, and a few days prior to that. This was probably due in some degree to the mental confusion, and not wholly to the loss of spinal-cord control, for after the confusion disappeared she gradually recovered this control. It is difficult to state whether the neurologic disturbances were due to central or peripheral changes in the nervous system. However, the disturbances of sensation including anesthasias, etc., were to some extent due to the neuritis which always accompanies intoxications of this class.

Opinions differ in regard to the action of carbon monoxide on

the human economy. Haldane has shown by experiments that all symptoms, immediate and secondary, can be referred to the want of oxygen, and that they vary according to the saturation of hemoglobin with the carbon-monoxide gas. He states that "With 20 per cent. saturation the only symptom is a slight tendency to dizziness and shortness of breath on exertion. As the saturation increases, however, the symptom of want of oxygen becomes more and more pronounced, until at 50 per cent. saturation it is scarcely possible to stand, and even slight exertion causes temporary loss of consciousness." In the fatal cases 80 per cent. of the hemoglobin is saturated with carbon monoxide. However, Le Dosseur sums up his conclusions as follows: "That in cases of survival, oxycarbon intoxication leaves frequently after it a series of complications bearing principally on the nervous system. The paralysis comes from cerebral and medullar lesions, or is due to the polyneuritis, or two other causes may come into play, traumatism and hysteria. The mental troubles are sometimes connected with material alterations in the brain, hemorrhages, thromboses, softenings. Sometimes they are completely independent. In all these cases the simple anoxemia of the red corpuscles is insufficient for explaining all the manifestations. Hysteria itself, though possible in certain cases, is unable to explain the phenomena observed. That experiments would tend to prove that carbon monoxide is dissolved in the serum and has a direct specific localized effect on the nerve cell." Mott is of the opinion that all the nervous symptoms can be explained by the thrombotic occlusions and hemorrhages which occur as the result of carbon-monoxide poisoning. These hemorrhagic conditions are more noticeable in the white matter of the brain, but this can be explained by the anatomical construction of the bloodvessels supplying these parts.

Unfortunately all observations of the course of such carbon-monoxide psychoses over a period of years is entirely wanting. Sachs in the preparation of his treatise on this subject was impressed by this fact, and states, "It would be interesting to know the further course of such cases." It is only in a mild uncomplicated case of this sort that we can make any regular comparisons as to its termination, as so many factors are to be considered. The majority of these cases prove fatal, and where this is not the case the mental symptoms vary from dementia to complete recovery. There are many things to be considered in the course and prognosis of the disease—namely, the general make-up and predisposition of the patient, the degree of poisoning, and in mine accidents we have to consider, in addition to the intoxication, the emotional stress, the overexertion and deprivations from lack of food and the exposure accompanying the trauma. Stierlin in his work gives a full report of observations made by himself and others among twenty-one survivors in the mine catastrophe at Caurrieres, on March 10, 1906, which claimed 1100

victims. These observations are of importance from the fact that they were continued over a period of two and a half years in the natural environments of the patients where they showed their psychopathologic conditions in the eccentricities of their lives and in their personal relations toward their families and friends. None of these patients made a complete recovery, although some of them were able to earn a living. The chronic effects of the intoxication, however, remained, which was shown by the neurologic changes as well as in the various forms of dementia present. He classified the mental phenomena into four groups, as follows, although none of them could be considered an entity, as each class encroached upon the other: (1) Psychoses caused by carbon-monoxide intoxication; (2) psychoneuroses caused by carbon-monoxide intoxication; (3) emotion psychoses; (4) traumatic neuroses of mixed etiology.

Mott calls attention to the fact that, considering the effect of carbon-monoxide poisoning being followed by mania, melancholia, confusion, and other mental symptoms, it must not be lost sight of that many cases to begin with are suicidal, and therefore if not actually insane at the time probably possess an insane or neuropathic temperament. This case was a pure and simple intoxication uncomplicated by any other neurologic factor. There was no inherited predisposition, nor was there present any deviation from the normal in her mental state previous to the trauma. She gave no evidence of emotional instability, had an even temperament, and was intelligent for one of her class. I am satisfied from the history given by her aunt and one of the servants who had been her friend for a number of years that suicide did not enter into this case. She was in an unusually happy mood previous to the poisoning, and besides this she was a devout Christian and always faithful in the performance of her religious duties. While the active mental symptoms abated in March she was not discharged until one month later, as her physical health was rather poor. Two months afterward she sailed to her brother's home in Ireland, where she has remained ever since. Inquiries made from her aunt show that the patient has written regularly to her relatives in this country, and there is no evidence from the content of her letters that she has undergone any change since she left. However, if the patient returns to this country the writer will endeavor to keep her under observation for some time.

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ACUTE POLYMYOSITIS.

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THE following observations were made upon a microörganism obtained by blood culture in this laboratory, upon a case of acute polymyositis, in the service of Dr. Charles K. Mills, in the University Hospital. The case itself will be put on record later.

A. G.; acute polymyositis. Material at hand consisted of scrapings and exuded serum from a papular skin eruption. Save for *Micrococcus epidermitis albus* in the scrapings, these were sterile. Two days later a blood culture was taken (3 c.c. blood to 200 c.c. +1 per cent. glucose bouillon). Specimens were again taken from the then rapidly drying cutaneous eruption, with the same result as above. From the blood culture a coccus was obtained corresponding to the one described by Martinotti¹ in a kidney abscess and named by him *Micrococcus polymyositis*. The organism in the fifth generation was agglutinated quite promptly, by the patient's serum. This coccus is in many ways identical with *Micrococcus pyogenes albus* and *aureus*, and for purposes of comparison a recently isolated strain of the latter was run through with the "polymyositis" organism from this case. The technical work is appended, and from it we conclude that the organism in question does not deserve a separate species name, the proper course being to speak of it as *Micrococcus pyogenes* var. *polymyositis*.

Biologically the culture which we shall call No. 5308 in this report differs from the usual forms of *Micrococcus pyogenes* only as follows: Upon plates and slants both of agar and gelatin it grows as a grayish-blue colony, and only in older cultures may one see a faint grayish-yellow color. It is never dense white or bluish-white. Liquefaction of gelatin is not so rapid in 5308 as in the *Micrococcus pyogenes*. No constant difference, such as in

¹ Zentralblatt f. Bakteriologic, etc., 1898, xxiii, 877.

stratiform or infundibuliform liquefaction, could be noted. Upon potato there is neither the intense orange of the "aureus" nor the porcelain appearance of the "albus." The medium is not colored. On milk the coagulation does not appear completed until the third or fourth day, after which the clot is so firmly contracted that a suggestion of digestion arises. This last, however, does not occur. It seems worthy of note that no growth was to be seen in the blood bouillon flasks until the end of the third day. These differences were observed in the third and tenth generations. The *Micrococcus aureus* used for comparison was also tried with the patient's serum. It was lightly agglutinated in the same time as a firm agglutination was observed with 5308.

The *Micrococcus aureus* and 5308 gave almost identical results when injected intraperitoneally into guinea-pigs.

In rabbits a subcutaneous injection of *Micrococcus aureus* gave a sharply outlined local abscess. Injections of 5308 produced a diffuse, boggy, tender swelling, with a slight reddening of the skin, all of which subsided in three days without rupture or general involvement.

Both cultures under consideration were injected into the circulation of rabbits, using a completely emulsified twenty-four hour agar growth. The height of the symptoms in the 5308 animal was apparently reached at the end of the second day, and on the third morning both were chloroformed. Martinotti describes a peculiar lameness and gait, and emphasizes the extreme sensitiveness of the animal. Both our animals on the second day were huddled down in the corner of the cage and refused to move, crying piteously if they were forced to do so. No particular differences could be noted other than the greater sickness of the *Micrococcus aureus* animal. Intravenous injections of *Micrococcus aureus* gave pyemia, with numerous sharply outlined muscular abscesses very irregularly distributed, abscesses of the lungs, heart muscle, liver, kidney, and a mild seropurulent peritonitis. Injections of 5308 intravenously resulted in a few abscesses in the liver and kidney, and a very slight early plastic peritonitis. In the muscles of the extremities, along the vertebræ and in the pectorals, there were found enormous numbers of minute diffuse, pale gray areas surrounded by a zone of hemorrhage and edema of varying width. In the other muscles these were less numerous. The lesions are more severe in the *Micrococcus aureus* animal, and while this may suggest a lower virulence of 5308, there is surely some degree of specificity or predilection for the musculature. The virulence of 5308 is less than that outlined by Martinotti for his culture.

Unfortunately for the continuance of the work no rabbits were available when these animals were killed, and when a week later we could obtain the animals the 5308 culture had lost its virulence entirely and would not infect them. Indeed, 5 c.c. were required to kill a small guinea-pig, and it did not seem worth while to sacrifice

animals further, since no increase was noted after two passages. It seems sufficiently proved that this 5308 is one of the *Micrococcus pyogenes* group, and should not be designated by a separate species name.

In a recent communication Schmitz² closely corroborates the above findings. There are a few noteworthy differences, however. His culture produced an intensely yellow growth especially upon ascites agar. My culture, now about nine months old, gave more pigment, a delicate yellow, upon serum agar than upon plain medium; at no time was the color intense. The virulence of his culture rapidly declined upon cultivation, and he noted a decline in virulence for rabbits in a re-isolation of the coccus from an abscess upon a guinea-pig isolated subcutaneously. He could, however, raise the virulence for rabbits by repeatedly inoculating them. His culture gave an infection picture close to that of Martinotti, but his control with *Micrococcus aureus* failed to show muscular involvement. Mayesima³ reports a case in which he isolated a *Micrococcus pyogenes albus* from the blood. He believes the infection atrium may be the tonsil.

This blood-culture finding is interesting from two standpoints: (1) It is another case to support the view that acute polymyositis is a bacteremia due to a micrococcus, with curious and rather uniform predilection for the musculature by which a subspecies or variety of a pus former can produce a definite clinical picture, with lesions more or less characteristic, and quite different from those produced by the most conspicuous member of the group to which it belongs. What determines the bacterium in its behavior is of course wholly unknown, and there is nothing in the clinical knowledge to help us. The infection atrium and the receptivity of the host probably play parts. It is suggested that the infection assumes the form of polymyositis when a *Micrococcus pyogenes* bacteremia occurs in a person whose condition favors rheumatism. There is of course no pathologic basis for this, as the lesions are different. F. Gottstein⁴ however, reports a case which was closely associated with one of acute articular rheumatism. Some attention is being given by the writer to the infections, particularly the subacute, in which pathogenic mutations are noted, and this case is but an example.

² Zentralbl. f. Bakt. u. Par., Original, Band 65, 259.

³ Deutsch. Zeitsch. f. Chir., 1910.

⁴ Deutsch. Arch. f. klin. Med., August, 1907.

CLINICAL IMPORTANCE OF REFLEX PHENOMENA IN INTRATHORACIC DISEASES, NERVOUS MECHANISM, AND DIAGNOSTIC LIMITATIONS OF REGIONAL MUSCLE CHANGES IN PULMONARY TUBERCULOSIS.

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In a recent communication¹ an historical *resume* of the literature relating to the sensory, motor, sympathetic, and reflex phenomena resulting from intrathoracic conditions was given. It was shown that both rigidity as well as degeneration of the muscles over the neck and thorax had been discussed by various authors prior to the time of Dr. F. M. Pottenger's announcement (1909). Balint, in 1903, and Jessen, in 1905, gave considerable data upon both these phenomena in connection with pulmonary tuberculosis. Balint particularly noted the rigidity, Jessen the atrophy of the trapezius. Remak reported rigidity of shoulder and arm muscles on the basis of reflex tonus from the inflamed lung. Musser, West, and others have noted the increased tension in the intercostals over an inflamed lung or pleura. Rigidity of the abdominal muscles as well as abdominal pain as a sign of intrathoracic inflammation has been observed by a great many authors, and is a matter of common knowledge. The myoidema, once regarded as a diagnostic sign of pulmonary tuberculosis, is to be regarded as a symptom only of atrophy, from what cause it gives us no information. Therefore we can state that muscle rigidity and degeneration in intrathoracic conditions is not a new discovery, but has been touched upon from time to time by many observers. That as a clinical sign of intrathoracic affections it is an entity cannot be denied. There are some clinicians who fail to perceive it, for them it does not exist, but there is no question but that careful palpation will demonstrate changes in muscular tension and "feel" in every case of pulmonary tuberculosis.

Cyriax, of London, also makes a claim to priority on the basis of statements made in *The Elements of Kellgren's Manual Treatment* in 1903. He stated, "Reflex contractions of the intercostal muscles result from many morbid conditions of the lungs, bronchi, and pleura." From what has been said such observations, however, were made prior to his writing.

I do not therefore regard these signs in the light of a recent discovery, but only a systematic exploitation of a clinical phe-

¹ J. L. Pomeroy, M.D., Critical Review of the Theory of Regional Muscle Rigidity and Degeneration in Intrathoracic Conditions, etc., Interstate Med. Jour., September, 1912.

nomenon which has been previously rather unsystematically studied.

In regard to the sensory phenomena in this disease, here too there have been many observations. Pain in diseases of the chest has long been recognized, and the earlier authorities thought it always due to pleurisy *per se*. Intercostal neuralgia was early recognized. Louis (1843) and Günsberg (1856) also described a hyperesthesia over the skin and muscles in the neck and back in pulmonary tuberculosis. Schmidt, in 1899, described various symptoms on the part of the sensory and sympathetic nervous system. He describes a neuralgic tenderness over the brachial plexus in apical tuberculosis, and noted paresthesias about the chest and arms, with hyperhidrosis and other disturbances. Many observers have reported evidences of peripheral neuritis, pains in the legs, arms, thighs, and other parts of the body (Beau, Leudet, and others). Pitres and Vaillard, in 1898, and Hammer, in 1899, investigated the question of peripheral neuritis in pulmonary tuberculosis, and found that there were three types: (1) Latent neuritis with no symptoms but neuritis demonstrated post mortem; (2) neuritis with sensory symptoms only; (3) neuritis with motor and sensory symptoms. In my own experience these disturbances are quite common, and at times troublesome to treat.

From a pathologic standpoint, while many authorities are conservative as to the neuritis being a specific result of the tubercle toxin, the weight of opinion is in favor of its being so. De Renzi observed degenerative changes in the phrenic nerve 27 times out of 29 cases; Jappa, Oppenheim, Steinert, Siemmerling, Cestan, and others have demonstrated degenerative changes in the peripheral nerves. Many other workers have confirmed these findings, and it seems to be proved that the tubercle toxin causes degenerative changes in the peripheral nervous system and in some instances even in the cells of the cord itself. Furthermore, irritative symptoms on the part of the toxin upon the brain and the meninges without actual tubercle formation have been observed. In some instances a mild meningo-encephalitis (not tubercle formation) was to be demonstrated. While in some instances the symptoms seem to rest upon the basis of a pure functional disturbance, probably due to cachexia and defective nutrition, the occurrence of neuritis in subjects where these factors did not exist is proof that they are not necessary causative agents.

The influence of alcohol, lead, syphilis, etc., is a difficult question to decide. While it must be admitted in certain cases that they do play a factor particularly predisposing, here again they are not necessary factors. I have seen a true Korsakoff (polyneuritic psychosis) and other neuritic symptoms in pulmonary tuberculosis where these factors were absent.

In regard to the phrenic, intercostals, vagus, and other nerve

fibers in the thorax, there is to be mentioned the effects of mechanical disturbance. Certainly the brachial plexus, the vagus recurrens (bronchial gland enlargement), and other nerves are involved in adhesions, etc., which cause deficient nerve function and peripheral and reflex phenomena.

Therefore it is to be concluded that while there is need for more definite anatomical research upon this question, it seems certain that pulmonary tuberculosis may cause definite degenerative changes in the nervous system; neuritis, posterior root inflammation, meningo-encephalitis, and other changes not due to tubercle formation, and further, these changes result not infrequently.

From the standpoint of reflex phenomena considerable work has been done. Prior to the time of the appearance of Head's classical schemata only desultory reports are to be found. Herpes zoster in pulmonary tuberculosis was frequently commented upon (Rendu, 1894, and others). Among the many reflex phenomena observed was pseudorheumatism of the shoulders (Bozzolo, Laserre), painful points about the apex and back (Schmidt, 1899), pain and tenderness in the intrascapular region, and over the second to seventh dorsal vertebræ (Petruschky, 1903, et alius), referred pain to the hypogastrium in diaphragmatic pleurisy (Günsberg, 1856, and Rosenbach, 1887). Sensitiveness to pressure and superficial hyperesthesia were noted by Walshe in 1860. Lange, in 1871, also described the referred pain to the epigastrium in diaphragmatic pleurisy. Cornet, in 1899, also mentions hyperalgesia over the affected area.

Furthermore, Würtzen, in 1906, gave an exhaustive review of the literature upon reflex hyperalgesia and pulmonary tuberculosis. His article and Schmidt's, in 1899, and the monograph of Jessen, in 1905, enable one to follow the literature almost to the present, and give vast sources of information. Francke, in 1908, demonstrated the close connection between the limits of the lesion by deep hyperalgesia, pressing the fingers deeply into the superficial tissues. Würtzen used only light touch with a blunt instrument, and showed close connection between the lung involvement and the hyperesthesia. He felt that this phenomena rested on the segmental theory of visceral reflex disturbance according to Head's zones. Head's zones were worked out on the basis of numerous cases of herpes zoster, and show the segmental areas upon the skin surface for pain, heat, cold, and trophic disturbances, and on the basis of various visceral diseases certain maxima are to be found in the skin. These zones are so well known that further elucidation is unnecessary. White and Van Norman recently have brought out a reflex hyperalgesia in the skin over the diseased lung, which limits itself only to the area involved. They give no mention of Würtzen, yet they have practically repeated his work. Wheaton, in 1910, claims to have demonstrated integument atrophy over the diseased area.

Head's reflex areas in connection with lung tuberculosis represent mainly the third to the fourth cervical zones, and the third to the ninth dorsal zones. When lower zones are stimulated he finds also the gastric factor in play, which would stimulate the same zones. Reflex disturbances also occur in connection with the fifth cranial nerve, with headache and tenderness. Jessen, Eggar, Goldman, also have studied this problem.

On the basis of these segmental studies it has been demonstrated that in pulmonary tuberculosis, one may find certain maximum points, often at the apex over the trapezius, between the shoulder-blades, tenderness over the vertebræ (frequently the second, third, and fourth dorsal), hyperalgesia over the second rib just inside the shoulder-joint area, points over the anterior part of the chest according to the seat of the lesion, also hyperalgesia of the skin proper, delimiting the diseased area, a deep hyperalgesia (Francke), an atrophic condition of the skin, sensitive areas over the abdomen (referred from the lower dorsal segments), and finally there may be referred disturbance in the region supplied by the fifth nerve over the head and face.

It is to be seen therefore that there are several factors in the problem of muscle change in intrathoracic lesions. The influence of the tubercle toxin on the peripheral nervous system, the mechanical influence in the thorax upon the nerves, and, furthermore, the reflex disturbances according to the segmental law of Head's zones. Recently, Harris brings forth a so-called diagnostic tender spot over the insertion of the levator anguli scapulæ in pulmonary tuberculosis. One may find many such tender points about the chest in intrathoracic disease, whether from tuberculosis or other conditions, and this sign is only a part of the complexes referred to, hyperalgesia. Alone such a tender point is of no diagnostic value in pulmonary tuberculosis.

Probably the most common areas of tenderness observed in connection with apical tuberculosis are over the middle of the trapezius ridge, over the brachial plexus area, the third and fourth dorsal vertebræ, and anteriorly over the second intercostal space near the sternum, and also to the inner side of the shoulder-joint on the chest. Where the disease affects the lower lobes we find tenderness over the fourth, fifth, sixth, and lower vertebræ, a tender spot at the lower angle of the scapula, in the axilla, and over the lower dorsal zones on the anterior part of the chest, and onto the abdomen. Often the points which show tenderness may be covered by a pin-head; again they are larger. They may indeed be bilateral in some instances. Between the shoulders over the rhomboidei and the levator scapulæ one not infrequently observes tenderness. A remarkable fact is that one observes these tender areas often at the earliest and again long after the patient is apparently well. In many instances there are no subjective symptoms

whatever, and their existence is unsuspected; again a dull boring ache may be complained of. Head states that the area of the second dorsal zone is commonly affected. Also the sixth dorsal segment. The two main points of this area are situated the one posteriorly at the level of the seventh dorsal spine, just internal to the angle of the scapula, and the other in front and under the breast. The lower area or the lowest two areas of the cervical plexus are also frequently affected. To these areas belong the tender points at the posterior aspect of the shoulder-joint, and those over the second rib and under the clavicle. Also the inner side of the arm and axilla.

When one considers the motor phenomena in pulmonary tuberculosis there comes into consideration the following: paralysis of the vagus recurrens; paraplegia; phrenic nerve paralysis; polyneuritis; changes in the distribution of the ulnar, peroneus, crural, and other nerves. Senator describes an interstitial myositis (gastrocnemius), with paraplegia. Balint noted changed electric reaction in the chest muscles over the affected lung; myoidema (Stokes, Tait, and others) was long held as a sign of pulmonary tuberculosis. Contractions and irritability and weakness of the orbicularis, the masseter, the sternocleidomastoid (Bozzolo), and atrophy of the trapezius over the affected area have been noted. Weakness of the voice is a common symptom. Several instances of phrenic nerve paralysis have been reported. (Vierordt, Rosenheim.)

Pottenger systematized the muscular phenomena and claims that by light-touch palpation one can pick out the diseased area in the lung by the condition of the overlying muscle tissue with a fair degree of accuracy. In early lesions the neck muscles, the trapezius, and muscles covering the apex are more rigid than normal. In late cases they become flabby and degenerated.

In regard to the atrophy of the trapezius, as described by Jessen, he considered that a local toxic diffusion in the muscles overlying the diseased lung only hypothetical, and with no substantial evidence to support it. He considered a latent neuritis to be a more plausible cause, and further felt that there might be some connection between the muscle atrophy and the segmental reflex phenomena after Head's theories. Pottenger believes that the muscle spasm results from the reflex excitation of the segments by afferent stimuli from the lung through the sympathetic nervous system to the cord, and their exciting neighboring centres in the anterior horns, with consequent spasm, as occurs in appendicitis, etc. Thus he explains the rigidity on the basis of Head's zones for visceral reflexes. The degeneration, he believed, was due mainly to overwork. I am inclined, however, to believe it to be of a trophic nature, from disturbance in the nervous mechanism in the spinal cord or in the nerve endings. Niehans in commenting

on the atrophy of the muscles about a tuberculous focus in bone tissue inclines to the toxic theory. The close segmental relation, however, between the nerves supplying the joint and the muscles moving the same would in my opinion be in favor of some nerve disorder of trophic nature.

In regard to the effects of the tuberculous toxin upon the muscles in pulmonary tuberculosis, Phillip regards the process as a progressive muscular dystrophy, in which all the muscles, somatic as well as visceral (heart, etc.), partake.

From the standpoint of trophic influence being the cause, particularly of the localized atrophy over the lung lesions, the findings of Gibson are of importance. Gibson (1911) agrees with Head and MacKenzie in regard to the segmental disturbances in angina pectoris, and further found, with Eichhorst, that in the painful areas, wasting of the muscles and changes in the texture of the skin, with increased myotatic, galvanic, and faradic irritability, were to be demonstrated. These observations distinctly support the theory that reflex disturbance of the cord through the sympathetics from the lungs will cause atrophy in the muscles corresponding to the segments affected.

When we come to consider the numerous sympathetic disturbances in pulmonary tuberculosis the theory of a nerve disturbance for the basis of muscle atrophy and rigidity gains more weight. Inequality of the pupils; flushing of the face, often unilateral; localized sweating (in hands, etc.); cardiac rapidity; pigmentation of the face and breasts; loss of hair; secretory disturbances; localized edemas in the skin, etc., and numerous other symptoms, all show the effect of the tubercle toxin on the sympathetic centres. The close relation existing anatomically between the inferior cervical ganglion and the pleura and the distribution of the sympathetic fibers from the anterior and posterior pulmonary plexuses show in part the pathway of these disturbances. Therefore, I believe there is sufficient ground to show that the disturbing stimuli pass through the sympathetic nervous system to the spinal cord (at least in part) and thus disturb the anterior horn cells, both as to muscle spasm, sensory phenomena, and subsequent atrophic changes due to trophic influence.

Furthermore, the sympathetic system has wide connections with the vagus, and this in turn secures a common origin with the ninth and eleventh nerves. A reflex disturbance therefore from the vagus can stimulate the muscles supplied by the ninth and eleventh nerves. The rigidity is particularly noticeable in the two muscles supplied by the spinal accessory, the sternomastoid, and the trapezius. Therefore, these muscles may be stimulated through central connections by the vagi or through the sympathetic connections with the spinal cord. The dilatation of the pupil, etc., show us that these centres in the cord are irritated, and it is only

carrying the process a step forward to conclude that the motor centres are also set into heightened activity.

Again, the recent work of Karsner demonstrates conclusively that vasomotor fibers exist in lung tissue about the pulmonary arterioles.

Another pathway for referred stimulation comes from the phrenic. This nerve has been shown to be frequently the seat of neuritis, and by its anatomical relations with the pleura is open to mechanical insult. Through its origin in the third and fourth cervical segments the muscles supplied by this segment are thrown into spasm (see these muscles in segmental charts). Capp's recent work further shows that the lower intercostals also enter into the supply of the diaphragmatic pleura, and through these, referred symptoms, muscle spasm and hyperalgesia over the areas corresponding to these nerves (in the posterior part of the thorax and the muscles of the abdomen also), may result. Head and others have long claimed that pleurisy does not cause referred or segmental disturbances. Capp's work, however, casts some doubt upon this. Pleurisy certainly must play some factor in the production of muscle spasm, and I believe that it does. The close anatomical relations of the pleura at the apex with the brachial plexus, the first intercostals, and the lateral intercostals also give rise to neuralgia, neuritis, referred pain, and other symptoms along the arm, the distribution of the ulnar nerve (elbow pain), and, according to Abrams, muscular spasm is a frequent accompaniment of intercostal neuralgia. Therefore, I believe that pleurisy does at times, according to its peculiar location, not only set up localized spasm but may give referred spasm over the abdomen and elsewhere. Certainly, disturbance of the diaphragmatic pleura gives tender points over the trapezius and muscle spasm in the area supplied by the third and fourth dorsal segments.

Schmidt's researches in regard to the apex of the lung and disturbance of the brachial plexus show that here also we may have a pathway for reflex disturbance. In pneumonia and pericarditis we also note referred symptoms over the lower intercostals onto the abdomen. The differentiation of intercostal neuralgia, neuritis, and pleurisy can only be made by considering the peculiar nature of the hyperalgesia and other symptoms which are characteristic of each. Nevertheless, Abrams reports cases where intercostal neuralgia simulates visceral disease, and advises freezing the nerve at its central origin in order to differentiate the nature of the lesion. In central disturbance the pain and spasm will not disappear, but in peripheral disturbance it will.

The communications of the two upper intercostals, and the intercostohumeral nerve explain the pseudo-angina or referred pain to the inner side of the arm so frequently seen in pulmonary tuberculosis. The deficient action of the diaphragm also may

be explained on the basis of irritation either of the lower intercostals involved in pleural lesions or direct insult to the phrenic at the apex or in the mediastinum.

The thoracic sympathetic system which joins the vagus to supply the lungs gives off branches from its upper ganglia to the spinal-root ganglia which supply the skin over the thorax. Through these fibers therefore we have a reflex pathway to the spinal cord for the production of hyperesthesia, hyperalgesia, and muscle spasm as well as trophic symptoms. The reflexes demonstrated by Abrams, brought about by percussing the vertebræ, or by irritation of the skin causing lung contraction or dilatation and similar phenomena in regard to the heart and aorta, support the view that we have definite reflex pathways for the intrathoracic viscera.

On the conception of the constriction of the chest in cardiac disease (angina), as brought out by Mackenzie, we may state that in pulmonary disease a persistent irritation of the sympathetic nerve conduces to the irritation of the spinal segment where the fibers for the lung connect with the spinal cord. Irritation of the sensory part of the cord conduces to sensation, which is projected into the periphery innervated by the nerves of the spinal segments. After this manner the motor and vasomotor symptoms are of like segmental character. We further know that counterirritation by a blister, etc., will reduce inflammation in the lung (Brunton). The occurrence of vertebral tenderness in early cases over the second or third dorsal vertebræ show the segments that are early disturbed. The lung receives its sympathetic fibers from the third and fourth cervical segments and from the third to the ninth dorsal segments (Head). From clinical studies the appearance of tenderness over the vertebræ, tender points over the anterior and posterior aspect of the chest, with skin hyperalgesia, we can state positively that proof of the irritation of the segments from the lung is conclusive. The sensory symptoms are only a part of a complex.

In affections of the lower lobes of the lung the lower dorsal areas are stimulated, and we obtain tenderness over the seventh, eighth, ninth, and tenth dorsal vertebræ, dull pain in the intrascapular area, and tender points in the axillæ, at the inferior angle of the scapula, and also anteriorly over the chest, and often on the abdomen. In some cases with these signs very little may be found on physical examination, the patient may consider that he has pleurisy, but no friction sounds will be heard. The x-rays will often show a high diaphragm and adhesions between the costal and diaphragmatic pleural surfaces with enlarged bronchial glands. These phenomena are much more commonly found than is recognized by the profession.

In many cases where gastric symptoms supervene one gets the

vertebral tenderness over the lower dorsal vertebræ and hyperalgesia in the corresponding segmental areas.

When we come now to consider the diagnostic importance of muscle spasm and degeneration, together with the concomitant symptoms, certain difficulties present themselves. This arises from the complex mechanism in the causation of these various symptoms. There may be neuritis, latent or manifest, with symptoms similar to intercostal neuralgia, or disturbances in the periphery also, the neurotic condition of the patient often exaggerates the picture. Also in a mechanical way symptoms may be produced by adhesions in the pleura, with various nerves, at the apex or in the mediastinum; and finally, we have the pure segmental disturbances. It is to be remembered that the heart, aorta, and bronchial glands may give rise to segmental reflexes similar to pulmonary lesions, and also in simple bronchitis reflex disturbances occur. According to some authorities emphysema and chronic bronchitis also are factors. Bronchial gland enlargement is more common than suspected, particularly in adults.

Differences in muscular development, occupation, posture, deformities of the spine, the condition of the superficial tissues of the chest (fat, etc.), age, nutrition, as well as certain diseases giving rise to muscular changes in the neck and thorax, all confuse the diagnostic importance of muscle spasm and degeneration in intrathoracic conditions. Spondylitis, Potts' disease, paralysis agitans, torticollis, rheumatic arthritis, disease of the middle ear, brachial neuritis, cervical rib, circumflex neuritis, aortic aneurysm are a few of the conditions which may give rise to reflex changes in the muscles over the thorax and neck, which are more or less permanent and will confuse the examiner.

Residuals from former conditions leave their impression upon the tissues of the chest. Pleuritis, pneumonia, asthma, bronchitis, pericarditis, etc., alter the mechanism of the respiration and the nervous and muscular actions.

Hence, muscle spasm and degeneration, as well as the sensory symptoms of intrathoracic disease to be used as a diagnostic aid in pulmonary tuberculosis, must be interpreted with extreme care. One must differentiate between eutaneous tenderness or hyperesthesia due to pleurisy, local neuritis, and hyperalgesia due to visceral disease and intercostal neuralgia. Reflexes from distant organs are also to be considered.

Marked destruction of lung destroys the nerve endings, and reflex symptoms may be absent. While the muscle spasm gives information as to the acuteness of the lesion or its activity, and degeneration, the age and chronicity of the disease, one cannot accurately localize the lesion in the lung on the basis of these signs. They will give a relative idea of its extent, but my autopsy findings show that it is inaccurate.

Consequently, it is only a rough and inaccurate index that inflammation is present in lung tissue or intrathoracic tissue. While White and Van Norman state that, according to their experience, the reflex hyperalgesia limited itself over the diseased lung tissue, in my observation, in comparison with autopsy findings in cases upon which I had studied the reflex hyperalgesia and muscle changes, these signs give only a hint as to the intensity of the inflammation and not the extent. In other words, the muscle spasm and degeneration as well as reflex hyperalgesia were observable in a limiting way, only over the intensely changed tissue, and did not clearly show the full extent of the lesion. From the very nature of the variations in the pathologic deposits in lung tissue the bizarre changes in anatomical relations occurring in advanced cases one could not expect from signs relating to nerve tissue, and reflex in character, to give accurate delimiting information. Therefore, the conclusion must be given that reflex hyperalgesia and muscle phenomena are only general in character, and any attempt to deduct information leading to accurate localization or limitation would be illogical and by practical experience, with autopsy comparisons, proved to be uncertain and misleading. Accordingly, one must consider these signs from the standpoint of an aid in clinical examination for localizing the lesion in the lung or thorax as of variable significance.

From the standpoint of the opinion of various authors who have written upon this sign the following extracts are given:

Hart claims that the conditions observed are not due to reflex causation, but result from overwork, as described by Freund and his followers. (See Pottenger's recent review.) He also raises the question of local toxic action, but discards it as being too selective.

Bonninger claims to have demonstrated a unilateral lymph stasis which causes the tissues to be firmer than normal. He rejects the reflex theory, and believes that disease of the underlying pleura was the cause.

Orzag confirms Pottenger's findings, but regards Balint's electric reactions over the diseased area as of more significance for diagnosis. He did not consider that the muscle spasm was of any value for early diagnosis.

Wolff-Eisner compared the muscle findings with the conjunctival tuberculin reaction, and concluded that the great practical worth of light touch palpation in the recognition of muscle change was "in the recognition of the initial active tuberculous process," and hence was of value from a therapeutic standpoint in pointing out the presence of active processes.

Bredow expressed doubt as to the value of muscle rigidity as described by Pottenger. He examined 107 cases of pulmonary tuberculosis and found only 7 in which the sign was present. Against

these 7 he was able to oppose 7 others which had the same rigidity, but in which careful examination elicited no indication of any lung disease. He concludes that the sign has no value in the diagnosis of tuberculosis. He also concluded: "That the symptom of muscular rigidity as an early symptom of disease of the lung cannot be confirmed. Differences in the state of contraction and consistency of the muscles of the thorax often occur. They are to be explained as a result of painful irritation, which necessitates holding one part of the thorax quiet, or as the effect of habit and occupation on the position of the upper dorsal vertebræ and on the structure of the upper thoracic aperture." I shall not attempt to enter into a discussion of these extracts, as Pottenger has discussed them in a recent communication.

Reflex muscle rigidity and degeneration as a sign of pulmonary tuberculosis is an interesting and important phenomenon, and when studied carefully in relation to the individual conditions gives considerable information regarding the stage of the inflammation. Its use requires close study and painstaking examination, and one unfamiliar with the technique will require long practice to obtain results. The reflex hyperalgesia, the tender points over the chest and vertebræ are also of interest and part of the general segmental disturbance. Careful examination will show their frequency.

It must be remarked that a careful estimation of the bearing of sensory and motor phenomena, particularly the referred type, is of importance from the standpoint of differential diagnosis. An understanding of the referred signs of intrathoracic inflammatory conditions, particularly pulmonary tuberculosis, in pneumonia and diaphragmatic pleurisy may clear up a doubtful case.

Abrams reports a case of intercostal neuralgia simulating tuberculosis and also a pleurisy simulating appendicitis.

Sahli states: "I have even seen gastro-enterostomy performed in cases of pulmonary tuberculosis on account of gastric symptoms and the appendix removed, because of radiating pleuritic pain without the trouble having been taken to examine the patients thoroughly." "*Difficile est satiram non scribere*" (Tuberculin Treatment, page 83). Therefore, a study of these reflex phenomena is of importance from a differential diagnostic standpoint, and will well repay investigation.

In regard to the sensory phenomena in connection with the diagnosis of pulmonary tuberculosis, the patient's subjective sensations are not to be lightly regarded. In many instances, pain, dull ache, feeling of heaviness, or other symptoms may be felt over an area, with little to be demonstrated on physical examination; yet later developments or the x-rays will reveal infiltration. Dunn, Minor, and Goodall have remarked upon the truth of these observations, and they must be borne in mind. Patients may

complain of more pain on the side where the pleura is least affected (Stanton). Again, one may find the pleura completely obliterated in subjects who have never had pain. We know that pleural adhesions occur in 99 per cent. of cases (at autopsy) always thicker over the apices and upper lobes. These variations in subjective sensations are important.

The fact is that subjective sensations occasionally precede the actual physical signs, and in this degree are important.

In the use of the muscle signs as well as the reflex sensory disturbances it is well to keep in mind the following statistics: According to J. Walsh, in 3144 cases the primary lesion was at the top of the right lung, the secondary lesion usually on the opposite side, and frequently more extensive. Barnes states of 860 patients admitted to the Rhode Island Sanatorium, 72.5 per cent had lesions in both lungs, of whom 56.6 per cent, were open. Hence, from the general history of the disease we would expect to find signs of the disease in most cases in both lungs.

In conclusion, it may be stated that various reflex phenomena occur in pulmonary tuberculosis, and muscle spasm and degeneration over the chest and neck are part of a complex which results mainly from a segmental disturbance through the thoracic sympathetic ganglia to the cord; but also irritation of the phrenics, the vagus, the brachial plexus, and the intercostals as well, unquestionably are factors in the presentation of the clinical picture. A localized neuritis from the tubercle toxin is also a possibility, while an actual diffusion of toxin in the area over the inflamed lung can only be surmised. There seems to be some definite relation between the diseased lung area and the muscle changes as well as the sensory electric reaction and trophic phenomena; the rigidity indicates activity of a recent nature, while regional degeneration indicates chronicity or destructive changes. Apparently no explanation seems more justifiable than that of a segmental disturbance after Head's generalizations. The frequency and constancy of disturbance in sensation, etc., over the chest and nervously connected tissues in intrathoracic disease seems to have been but little recognized by the general profession.

A search of the literature, however, reveals that a number of authors have studied these phenomena, and it remained for Pottenger to systematically study the motor reflexes, which he has ably done. From the standpoint of the early diagnosis of intrathoracic affections, particularly pulmonary tuberculosis, from the fact that these phenomena are by no means uncommon, and possess interesting variations, the study of the sensory and motor reflexes from the chest recommends itself.

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REVIEWS

A TEXT-BOOK OF PRACTICAL THERAPEUTICS, WITH ESPECIAL REFERENCE TO THE APPLICATION OF REMEDIAL MEASURES TO DISEASES AND THEIR EMPLOYMENT UPON A RATIONAL BASIS. By HOBART AMORY HARE, M.D., B.Sc., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital; One-time Clinical Professor of Diseases of Children in the University of Pennsylvania, etc. Fourteenth edition; pp. 984; 139 illustrations. Philadelphia and New York: Lea & Febiger, 1912.

WHEN in less than twenty-two years a book reaches its fourteenth edition, there is little need for the reviewer to attest its value. Such a record furnishes the most gratifying proof of the popularity and enthusiasm with which Hare's *Practical Therapeutics* has for years been received by the medical profession. This new fourteenth edition, however, merits comment because it has actually been thoroughly revised and largely rewritten, so that it presents the treatment of disease in accordance with the most modern teaching.

In the general make-up, the new edition is not unlike the earlier ones, the book being divided into four parts. Part I takes up general therapeutical considerations. Part II deals with drugs which are arranged alphabetically; under each drug is given its occurrence, its physiological action, its therapeutic uses and toxicology, and its preparation. Part III is particularly valuable, since it covers all the important remedial measures other than drugs, such as antitoxin, hyperemia, cold and heat, hydrotherapy, exercise, climate, diet, etc. Part IV is devoted to the treatment of disease; important diseases and symptoms being arranged alphabetically, and under each the most approved methods of treatment are given.

Of late years much noteworthy experimental work has been done upon the pharmacodynamics of many drugs. It is gratifying, therefore, to note that in this edition the accounts of the physiological action of the important drugs has been revised in accordance with the latest observations. This is especially true of digitalis, caffeine, and alcohol. Notable additions to the text are also the section on Bier's treatment by artificial hyperemia,

the use of tuberculin, vaccine therapy in general and the principles upon which it is based, and the employment of salvarsan.

Over a quarter of a century of continuous activity as clinician, investigator, and medical teacher has enabled the author to appreciate with unusual clearness the needs of the practitioner. As a consequence, in the present edition of his book, Hare has so skilfully correlated the results of laboratory investigations with clinical observations that we know of no other book in which the relationship between the scientific and practical aspects of therapeutics is made so clear or to which the physician at the bedside may turn with greater assurance of finding the help which he seeks.

G. M. P.

MANUAL OF HUMAN EMBRYOLOGY. By Fifteen Writers. Edited by FRANZ KEIBEL, Professor in the University of Freiburg, and FRANKLIN P. MALL, Professor of Anatomy in the Johns Hopkins University, Baltimore. Volume II. Pp. 1032; 658 illustrations. Philadelphia and London: J. B. Lippincott Company, 1912.

AN important stage in the progress of the science of human embryology is marked off by the appearance of Keibel and Mall's work, the second volume of which is now before us. The attitude of one of the editors (Professor Mall) toward his subject is thus expressed in a recent article. "Gross anatomy as a science is bankrupt. It is made solvent through embryology which alone illuminates it." And, again, "a great field opens to us for the study of histogenesis which binds embryology to histology, to make the foundation for scientific anatomy." When such is the enthusiastic point of view, the result cannot fail to be a notable production. The work is complete in two volumes and has appeared at the same time in an English and a German edition. It is also international in character in the personnel of the contributors, for of these six are European and nine are American. The first volume was published in 1910 and the present one in 1912. The plan of the work is on the "Handbuch" type, inasmuch as small subdivisions of the subject are treated by different authors, each of whom has special knowledge of the field of which he writes.

The present volume contains seven chapters numbered XIV to XX. The development of the nervous system (Chapter XIV) is considered under the four headings: (1) histogenesis of nervous tissue; (2) development of central nervous system; (3) of peripheral nervous system, and (4) of sympathetic nervous system. Chapter XV treats of the chromaffin organs and the suprarenal body, of which only the medulla is formed of chromaffin tissue. This tissue is described as secreting a substance which produces contraction of the non-striped musculature, and especially serves to maintain

blood pressure and vascular tonus at corresponding levels. The largest of the separate chromaffin organs are the aortic bodies (of Zuckerhandl), which measure in the newborn child, 11.6 mm. on the right side and 8.8 mm. on the left side. They are situated laterally to the aorta, near its point of bifurcation. Their size becomes less in post-fetal life but they do not actually disappear. Chapter XVI describes the development of the sense organs and Chapter XVII the digestive tract and the organs of respiration. In Chapter XVIII, are included the blood, the vascular system, and the spleen. Professor Minot, in his description of blood, considers that red and white blood corpuscles have the same origin, or in other words, arise monophyletically, and in this he is in agreement with a number of recent investigators. The primitive cells from which all are derived he terms "mesameboids," and some of the descendants of these continue throughout life to have the same embryonic character, and so to serve as the source of the new blood cells. Since they can move freely they can alter their distribution in the body. At one period of fetal life they are in the liver and lymphoid organs, but finally, they migrate into the marrow of bones, and thenceforth this serves as the permanent site of blood formation. He adds, however, that this view is not secure beyond all doubt. All leukocytes, accordingly, have a unitary origin also, and Minot thinks that they develop from the primitive mesameboids, but admits that investigators are divided on this point. The other view is that free wandering cells (leukoblasts) arise directly from mesenchymal cells. Four principal classes of leukocytes are recognized: I. Young forms without granules (lymphocytes); II. older forms with granules—(a) finely granular (neutrophile of Ehrlich); (b) coarsely granular (eosinophile of Ehrlich); (c) degenerating (basophile of Ehrlich). Of these the finely granular leukocytes represent the chief developmental series of the white corpuscles. The blood vascular system by Dr. H. M. Evans, is based, for the most part, on the beautiful series of injected specimens of young embryos, which he has himself prepared. In the consideration of the lymphatic system, Professor Sabin clearly defends her view that the lymphatic system arises from veins, and that the lymphatics grow out by the sprouting of the endothelium of preceding vessels. In Chapter XIX there is a comprehensive account of the urinogenital organs, and the final chapter is devoted to a short account of the interdependence of the various developmental processes.

Throughout the authors have presented the results of numerous investigators with careful judgment, and these have been verified and supplemented by much original work. The result is a repository of knowledge on human embryology, which must be of the greatest value to every student of the sciences, and which will undoubtedly serve as the starting point for many new researches.

W. H. F. A.

COMMON DISORDERS AND DISEASES OF CHILDHOOD. By GEORGE FREDERIC STILL, M.A., M.D. (Cantab.), F.R.C.P. (Lond.). Pp. 813, illustrated. Oxford University Press, 1912.

THE second edition of a book so highly successful needs but little comment. As the author states in the preface to the first edition, the book is no systematic treatise, but deals mainly with the everyday and the commonplace. Nothing, however, is lost by this method of treatment and much is gained; each subject discussed is treated as an entity and there is none of the inconvenience of unimportant detail. In the present edition several new subjects have been added, among which may be mentioned enlarged tonsils and adenoid hypertrophy, epilepsy, asthma, and hydrocephalus; while the sections on infantile paralysis and congenital syphilis have been rewritten.

Of the new sections, that on enlarged tonsils and adenoid hypertrophy is admirable and thorough. Not only is the importance of these conditions fully emphasized, but many facts not usually thought of in this connection are mentioned. The author is conservative as to operative treatment, but insists on thorough removal when operation is advised. The chapter on asthma is not so happy, but does properly emphasize the danger of resulting emphysema in chronic cases which is often neglected in works on diseases of children. Of the old chapters those on rheumatism and on jaundice in children stand out among many as especially helpful, and in them, as indeed in the whole book, the reader feels the personality and experience of the author, and rather than adversely criticise the frequency of "I think" and "In my experience," one is tempted to attribute to this very fact, a part at least, of the charm and value of the book.

O. H. P. P.

PSYCHANALYSIS. ITS THEORIES AND PRACTICAL APPLICATION. By A. A. BRILL, Ph.B., M.D., Chief of the Neurological Department of the Bronx Hospital and Dispensary. Pp. 337. Philadelphia and London: W. B. Saunders Co., 1912.

PSYCHANALYSIS is receiving constantly more and more attention not only from the medical public but also from the laity. Therefore it is not at all surprising that one of the leading exponents of Freud's theories should bring out a book on the question. This work is a brief *resume* of Freud's ideas, each important division being treated in a chapter. Most of the material has been previously published.

To understand fully the present American view of psychanalysis it might be well to trace it from its beginning. Philadelphians,

for example, prefer to treat nervous patients with the so-called rest cure and incidentally practice psychanalysis, but the rest cure with psychanalysis by trained neurologists is quite a different matter from that practised by one who is not trained in neurological lines, and as a consequence throughout the country every medical practitioner has the idea that to cure a nervous patient all he has to do is to put him to bed, feed him up on milk and eggs, and so far as his mind is concerned—why that will take care of itself (as if a mind could take care of itself) and as a consequence what resulted? Christian Scientists. This, however, like so many things, only fills one phase of the question, for they have made the mistake that some rest curists have—they have neglected the physical, while the latter neglect the mental. Now, we are having a combination in the osteopaths, chiropraths, Bohemian thrusters, while in latter days it has become the fashion to treat all diseases either by venoms, serums, or polyglandular extracts. It is no wonder that we are still seeking for a method.

Freud himself, before he elaborated his present method, was a well trained neuropathologist and neurologist. His disciples either accept everything he states without question or attempt, as much as their limitations allow, to come as near it as possible, and the consequence is that Freudian doctrines are being practised only by a few men as they should be. In Europe the acceptance of Freudian theories has not been by any means uniform, but it has been accepted by some of the best neurologists. The basis of the whole contention is that to Freud every neuroses has a sexual origin. Some of his critics state that inasmuch as Freud practises in Vienna he is judging the entire universe by this city, which is notoriously sexual. What some of these critics should do is to live for a short time only in New York, Chicago, San Francisco, or even in Quaker Philadelphia, and then they would not accuse Vienna of having a monopoly. However that may be, in this country Freudian doctrines have been only very slowly accepted. About three years ago, in a discussion of the subject before the American Neurological Association, there was almost a universal condemnation of it, and it cannot be said that many gains have been made in its adherents since then, and perhaps 90 per cent. of neurologists condemn it without hesitation. If, therefore, 90 per cent. of neurologists condemn such a method, what can be said of the general practitioner or the internist who are even less qualified to judge Freud's doctrines. The basis of the whole thing after all is that the average physician hates to think, as would the average intelligent layman, that all neuroses have a sexual cause. The idea is so absolutely abhorrent to most decent living men that with almost one voice they say, "Filth, filth, nothing but filth." Now let us try to analyze the situation calmly and see if it is all filth.

Freud's conception of the sexual is very broad, and quoting from Brill, "It is just as broad as our English word love or the Greek word 'eros,' and does not at all limit itself to the gross sexual. Moreover, it must be remembered that sexuality is more complicated than one thinks." Freud further states "that the newborn child brings with it the germs of sexual feelings, which continue to develop for some time and then succumb to a progressive suppression, which is, in turn, broken through by the proper advance of sexual development and which can be checked by individual idiosyncrasies." In other words, Freud does not mean that by the sexual you or breaking the Seventh Commandment. If, therefore, one looks at it from a broad standpoint, one is compelled to admit that the strongest passion and the strongest impulse is the sexual and that it dominates every man and every woman. Why not, therefore, admit it? Is it unusual when considering the education of a child in sexual matters, that the constant "don't do this and don't do that" which accompany the growth of an individual should sometimes cause neuroses? After all, we are a race of prudes. We do not educate our children properly. We tell them all about the breeding of cats, dogs, and horses, we teach them the dangers of typhoid fever and smallpox, but, do we teach our children anything about gonorrhea or syphilis? Why not therefore admit it at first hand that it is no wonder that the sexual, looking at it in a broad way, can cause all sorts of neuroses.

So far as abnormal sexual practices are concerned everyone knows, who knows anything about life, that the abnormal sexual is quite common in the so-called normal individual. Every doctor meets with it and there are some who think it is on the increase. However that may be, on every hand one is constantly confronted with the sexual. We find in it our theatres, dramas, divorce courts, everywhere. The conclusion, therefore, must be reached that Freud is right and the sexual in a broad sense can cause and must cause all sorts of repressed ideas and neuroses. The wonder is not that it does, but why someone has not called attention to it before. The reviewer is, however, by no means prepared to admit, as Freud does, that every neurosis has a sexual basis, but he admits willingly that a great many have this origin.

Now as to what these doctrines have done and why they are gaining favor. We have been accustomed to treat our nervous patients as a class. We give them bromides, we tell them to forget their troubles (we never tell them how, by the way), we call their troubles "only functional," as though functional diseases were so easy to get rid of, but we have not done what common sense would indicate—we have not treated patients individually. Everyone must admit that no one person is like another. No person's education is like another's, and yet we have not treated

individuals as individuals, which is what Freud does, and, therefore, in that one respect alone he has done a great deal of good. Again, take his views of dementia præcox and the different delusions, hallucinations, mannerisms, and stereotyped movements that these patients have. Instead of accepting the old time idea that a patient has delusions and hallucinations because he is a case of dementia præcox, Freud states that the type of delusions and hallucinations are dependent upon the individual's previous personal history. This is nothing more than common-sense.

As for Brill's book. He states in his preface that "one cannot expect to become proficient in psychoanalysis unless he has mastered at least Freud's theories of the neuroses, the interpretation of dreams, the sexual theories, the psychopathology of everyday life, and his book on wit, and last but not least, who has not a training in nervous and mental work," and then he proceeds to write a book on Freud's theories in 325 pages. He further states that: "These assertions are not based merely on the reading of a few scattered papers, but on about six years of hard work and almost constant occupation with the subject. For it is only through hard work and long experience that one can acquire a thorough knowledge of Freud's psychology." How can he expect, therefore, that the neurologists who instinctively oppose Freud's ideas will get anything out of such a work and what can be said of the general practitioner who knows less. Certainly, after reading such a work as this with no previous knowledge on the subject, it is no wonder that most physicians are filled with loathing that such a thing is possible. It is a pity that this work should have been published. It would have been far better if the author had produced only one of the fundamental theories at a time. Of course, the answer can be made that this has been done by the author himself in his translations as published by the *Journal of Nervous and Mental Disease*, and if so, there is hardly any need for this book, because it does not do what every book should do. It does not adequately explain the subject. One thing perhaps has been accomplished; it has called attention of the medical public to the importance of the sexual in the formation of the neuroses.

T. H. W.

FIFTH SCIENTIFIC REPORT OF THE INVESTIGATIONS OF THE IMPERIAL CANCER RESEARCH FUND. By E. F. BASHFORD, Director. Pp. 94; 13 illustrations and numerous charts. London: Taylor & Francis, 1912.

THE report consists of four papers on the experimental investigation of cancer. The first paper is by B. R. G. Russell on "The

Manifestation of Active Resistance to the Growth of Implanted Cancer," and demonstrates that the power of producing immunity appears to be a part of the parenchyma of the tumor, and that it also is influenced by the soil exhibited by the inoculated animal; simultaneous inoculation of a tumor strain that rapidly induces resistance can retard the growth of grafts from a strain which tends to grow progressively; it has also been shown that mice bearing progressively growing tumors can be immunized against re-inoculation, even although this immunity does not, as a rule, inhibit the further development of the tumor already established.

The second paper, written by Wm. H. Woglom, on "The Nature of the Immune Reaction to Transplanted Cancer in the Rat" is rather controversial in nature and supports the contention of Russell as against that of Burgess, concluding that the phenomena described by Russel as characterizing the immunity of mice to tumor implantation occur also in the case of the resistance offered by rats to the Flexner-Jobling adenocarcinoma.

The third paper, by C. da Fano, on "A Cytological Analysis of the Reaction in Animals Resistant to Implanted Carcinomata" would indicate that the polymorphonuclear leukocytes and the lymphocytes are most important in the local cell reactions of immunized animals.

The fourth paper, by S. Higuchi, "On the Immunizing Power of the Placenta, Blood, Embryonic Skin, Mammary Gland, and Spleen of Different Species against Carcinoma of the Mouse" shows that the strongest immunity is produced by homologous tissues, that killed tissues produce no immunity, and that homologous spleen can produce an immunity which reaches its height in ten to twelve days following the injection.

All the papers presented are concisely and clearly drawn up, are well illustrated by drawings and charts, show keen insight into the problems studied, and can be read with pleasure, interest, and profit even by those whose special lines of endeavor do not coincide with those of the authors.

H. T. K.

DISEASES OF CHILDREN. By BENJAMIN KNOX RACHFORD, M.D., Professor of Diseases of Children, Ohio-Miami Medical College, Department of Medicine of the University of Cincinnati, Pediatrician to the Cincinnati, Good Samaritan, and Jewish Hospitals, Cincinnati. Pp. 783; 107 illustrations and 6 colored plates. New York and London: D. Appleton and Company, 1912.

THE importance of pediatrics as a special branch of medicine is being emphasized by the rapid additions to pediatric literature

of such treatises as this volume, wherein the whole subject receives thorough orthodox treatment while there is shown throughout the individual stamp of the author's personal judgment and opinion. The book is essentially practical. Pathological findings are but briefly outlined and unnecessary etiological discussions are avoided in order to afford space for an ample consideration of diagnosis and treatment. In addition to routine subjects we find a consideration of otitis media and mastoiditis, and of the common diseases of the skin.

Among the introductory chapters the section on excessive nerve activity is particularly timely. The danger of overstimulation and forced development of the child's brain in these days of nervous instability cannot be too strongly emphasized, and the note of warning gains in value coming from one so well qualified to sound it as the author.

Of much value, also, are the chapters on treatment wherein are discussed various measures, medicinal and others, as they apply to infancy and childhood. Exception might be taken to one statement to the effect that rest in bed in acute nephritis should be insisted upon until the urine findings are normal. While this is undoubtedly sound teaching in a majority of cases, yet its strict and literal enforcement in all would prolong the rest-period to an unjustifiable length, with actual harm to the child's other functions.

The important chapters upon feeding, with a careful consideration of the relations of milk to the child's nutrition, are notably clear, practical, and sensible. No subject is more difficult to present, and much that has been written in recent years has failed to accomplish its mission because of what might be termed its technical difficulties. These the author skilfully avoids. To many pediatricians it will seem that he has accorded to condensed milk and proprietary foods a much more definite place in the dietics of infancy than they deserve. This is unfortunate, since it will furnish students and practitioners with an additional excuse for the use of these undesirable substitutes for good cow's milk.

The author's conception of the various disorders of digestion and of the organs of digestion, is conservative. He avoids the extremes of the Continental school while recognizing the value of their teaching, and refuses to relinquish the lessons of years of experience for the somewhat theoretical views promulgated within less than a decade.

In the case of appendicitis it might be objected that he somewhat overemphasizes the value of "medical treatment" and places the burden of decision "when to operate" an unduly long time upon the shoulders of the physician.

Especially able are the chapters upon tuberculosis, and the lessons which he teaches could well be learned by many who are inclined rather to the belief that their student days have passed so far as clinical medicine is concerned.

To sum up, it may be said that the book is conservative while it includes all that is worthy of acceptance; and that the great care given to diagnosis and treatment make it of particular value to the practical physician in search of enlightenment and guidance.

J. C. G.

ELEMENTARY BACTERIOLOGY AND PROTOZOÖLOGY: THE MICROBIOLOGICAL CAUSES OF THE INFECTIOUS DISEASES. By HERBERT FOX, M.D., Director of the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania. Pp. 237; 67 engravings and 5 colored plates. Philadelphia and New York: Lea & Febiger, 1912.

THE discussion of a technical subject in terms which will be intelligible to the person without technical training is always very difficult. In the task, therefore, which Dr. Fox has set before him, there are many pitfalls.

This work of 237 pages is the author's maiden effort in extended publication, his object being "to give the nurse and the beginner an idea as to the nature of microorganisms and their relation to the world's economy, especially disease." There are fifteen chapters, a glossary, and a fairly full index. The arrangement of the subjects included under the general term of microbiology is good, though in the descriptions and discussions the work occasionally shows some of the faults common to many first editions, such as involved sentences and a few typographical errors. The illustrations are good though not original. When one considers the difficulty of preventing a work of this kind from becoming too technical for the average nurse or lay person, and too general for the student or nurse, going more particularly into bacterial or protozoal work, it must be admitted that the author has for the most part steered a safe middle course. The book should certainly supplant the many elementary works on this subject now in use.

F. H. K.

X-RAY DIAGNOSIS AND TREATMENT. By W. J. S. BYTHELL, B. A. Cantab., M.D. Vict., Hon. Physician to the Ancoats Hospital, Manchester (Electrotherapeutic Department); Medical Officer to the X-ray Department of the Manchester Children's Hospital and the Salford Royal Hospital, and A. E. BARCLAY, M.D., Cantab., M.R.C.S., L.R.C.P., Medical Officer to the Electrical and X-ray Departments Manchester Royal Infirmary, etc. Pp. 147; 118 illustrations. London: Henry Frowde and Hodder and Stoughton, 1912.

THE main object of this book is to acquaint the medical practitioner with the uses of the x-rays in diagnosis and treatment, and

to enable him to select those cases in which x -ray therapy or examinations are applicable or indicated. For this reason very little attention is paid to the details of manipulation of apparatus, technique, or the phenomena of x -ray production which characterize those works intended to appeal especially to the specialist in Röntgenology. A few pages are devoted to a brief presentation of salient facts concerning the production of x -rays and descriptive of the apparatus required. Most of the book is given up to the diagnostic side of x -ray work, and following the chapter covering each subject, are a number of excellent reproductions from radiographs of illustrative cases. Because of the wide scope of the subject as a whole and the limited space in the book, some of the chapters have had to be very brief, from the standpoint of the Röntgenologist, at least, and especially the one dealing with the diagnosis of abdominal conditions. However, each subject is covered in such a way as to acquaint the general practitioner with practically all of the applications of x -ray diagnosis. The short chapter devoted to x -ray therapy can do little more than outline the conditions in which this therapeutic agent is applicable, or can be used to advantage.

H. K. P.

DIE ENTSTEHUNG DER KURZSICHTIGKEIT. Von DR. GEORG LEVINSOHN, Privat-Dozent für Augenheilkunde an der Universität Berlin. Mit 3 Abbildungen im Text. Pp. 88. Verlag von S. Karger, Karlstrasse 15, Berlin, 1912.

FROM a critical examination of the views commonly held in regard to the cause of myopia, the author concludes that neither the accommodative act nor pressure from the external muscles in convergence or lateral movements are capable of bringing about the changes observed in myopia. Experiments with the manometer in animals' eyes and the tonometer in the human fail to show the slightest change in the tension in all positions of the eyeball. Moreover, universal experience shows that the effect of increased intraocular tension is productive of changes quite different from those observed in myopia.

The author makes an exhaustive study of the fundus changes in myopia (conus, staphyloma posticum, supertraction, etc.). Emphasis is laid on the great difficulties and even impossibility of accounting for the observed anatomical changes by any of the common hypotheses.

A really effective hypothesis which shall actually account for the genesis of myopia must be based upon some influence which comes into play during near work; and as he believes to have

demonstrated that no such power can be found in the accommodation, convergence, or the lateral movements of the eyes, but a single factor remains, and one which, strange to say, has been almost unnoticed as the determining element. This factor is represented by the bending forward of the head and trunk, a factor which, he believes, exercises a very important influence upon the lengthening of the youthful eyeball. By such bending forward of the head, the globe, which is rather securely fixed in all directions, except from before backward, becomes subject to the influence of gravity which force necessarily tends to draw the eyeball forward and drag upon its connection with the optic nerve.

To demonstrate the effect of the force of gravity in the bending forward of the trunk and head the author devised an apparatus attached to the bony entrance of the orbit. From the tracings found with this it could be readily seen that the eyeball sank downward and forward upon bending the head and trunk and that such sinking was exactly proportional to the degree of the inclination of the head. The increase in the amount of blood in and especially behind the eyeball during such forward movements of the head and trunk will also affect the position of the eye to an appreciable extent and be an accessory factor in the sinking forward of the globe.

Such, in short, is the hypothesis which Levinsohn sets up for the solution of the problem of the genesis of myopia. The fact that a new hypothesis seems necessary is sufficient evidence that this important question is still *sub judice*. Whether the new hypothesis is really the long sought for solution remains to be seen.

T. B. S.

THE WASSERMANN REACTION. By JOHN W. MARCHILDON, B.S., M.D., Assistant Professor of Bacteriology, St. Louis University Medical School.

THIS new book on the Wassermann reaction by John W. Marchildon, covers in detail the methods of preparation of the various reagents and the technique of the reaction according to Wassermann's original teaching.

There are a number of errors in this technique and its interpretation, and a few confusing errors in the printing.

The book concludes with a brief but clearly written discussion of the clinical value of the Wassermann reaction in the various stages of syphilis, in parasyphilitic conditions, and in diseases other than syphilis, and the effect of the different forms of anti-syphilitic treatment on the Wassermann reaction, in which are many statements of value to the clinician.

J. F. L.

HANDBUCH DES GESAMTEN MEDIZINISCHEN ANWENDUNGEN DER ELEKTRIZITÄT EINSCHLIESSLICH DER RÖNTGENLEHRE. Professor Dr. Med. H. BORRUTAU, Privatdozent f. Psychologie an der Universität Berlin; Professor Dr. Med. L. MANN, Privatdozent f. Nervenheilkunde an der Universität Breslau; Professor Dr. Med. M. LEVY-DORN, Leitender Arzt am Rudolph-Virchow-Krankenhaus in Berlin; and Professor Dr. Med. P. KRAUSE, Direktor der medizinischen Universitätsklinik in Bonn. Vol. II, second half, pp. 1102; 292 illustrations. Leipzig: Werner Klinkhardt.

THIS is the second half of the second volume, and is the last of the three volumes which constitute this monumental work upon the medical uses of electricity. The previous two volumes have been reviewed in this JOURNAL. Altogether, these three volumes comprise everything in the literature on the technical and therapeutic application of electricity. It is such a work as is possible to be produced only by the Germans, and is the best work on the subject.

The first volume consists of the introductory chapters on electricity and magnetism, the physiological chemistry of the influence of electricity on the human being, theories of electrical irritation, its physiology and pathology, and a beginning description of the technique and apparatus. The second volume embraces the diagnostic points of the different forms of nervous disease which are applicable to therapeutic electrical treatment. It is practically a nervous diagnosis. The third volume, and the most important one, discusses general electric therapeutic application, and is complete in every sense. It discusses principally nervous diseases, but also includes chapters by various individuals who have made specialties of such particular subjects as the heart, rhinolaryngological diseases, the eye, ear, skin, diseases of women, joint and muscle diseases, static applications, high frequency currents, uses of electric light and heat, electrolysis, cataphoreses, galvanism and phototherapy.

T. H. W.

AIDS TO OPHTHALMOLOGY. By N. B. HARMON, M.D. Pp. 216; 100 illustrations. New York: Wm. Wood & Co., 1912.

IN this work the attempt is made to cover the subject of ophthalmology in the space of two hundred pages. Any such endeavor must fall short of obtaining the desired end, and result in a work of limited usefulness. The post-graduate student, for whom the author specifically wrote this book, would, we feel, be investing his time without obtaining a just proportion of thorough information by devoting his attention to Harmon's work. B. F. B. JR.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Bence-Jones Proteinuria in Conditions Other Than Myelomatosis.
—BOGGS and GUTHRIE (*Johns Hopkins Hosp. Bull.*, 1912, xxiii, 353) have found in the literature instances of Bence-Jones proteinuria in conditions other than myelomatosis. These included a case of osteomalacia, 1 of gun-shot wound of the leg, and 3 cases of lymphatic leukemia. The only instance of metastatic bone carcinoma was a case of gastric tumor reported by Oevum. The authors report an instance in a woman with primary carcinoma of the breast and metastatic dissemination in skull, ribs, both trochanters, both ilia, and right tibia. They are struck with the fact that all the cases have one point in common—the more or less extensive involvement of the bone marrow. It is also obvious that the relation of multiple myeloma to Bence-Jones proteinuria cannot be specific. Other disease processes involving the marrow may lead to the excretion of this unusual body. The excretion of the protein seems also to bear no fixed relation to the extent or duration of the disease process, as it may occur in the urine before any demonstrable bone lesions may occur, and may disappear at a time when the lesions in the marrow are most extensive. Again, very widespread involvement of the bone marrow may occur unassociated with this type of proteinuria.

The Mechanism of the Tuberculin Reaction.—F. MEYER and K. E. F. SCHMITZ (*Deutsch. med. Woch.*, 1912, xxxviii, 1963) report an experimental study of the tuberculin reaction. They infected four rabbits with bovine tubercle bacilli (*Perlsuchtbacillen*). At varying intervals after the infection became well established, they withdrew

blood from the ear vein. Whole blood, serum, and washed corpuscles were then incubated for a short time with bovine tuberculin (Perlsucht-tuberkulin), and the mixtures, often after standing twenty-four hours in the ice chest, were injected into normal rabbits. Tuberculous serum plus tuberculin, with or without the addition of complement, may produce a febrile reaction when injected into a normal animal. The reaction is more marked when whole blood or washed corpuscles from a tuberculous animal is incubated with tuberculin and then injected intravenously into normal rabbits. Fever, dyspnea, prostration, and sudden lowering of the temperature may follow. As controls, the blood and corpuscles of normal rabbits incubated with and without tuberculin, and tuberculous blood and corpuscles incubated without tuberculin were used. Only minimal rises of temperature were observed which subsided rapidly. It was shown that the toxic substance which is formed during incubation of washed corpuscles and tuberculin may pass into the salt solution in which the corpuscles are suspended.

The Origin and Significance of Basophilic Granules in the Erythrocytes.—M. GEORGIOPOULOS (*Wien. klin. Woch.*, 1912, xxv, 1704) has made observations on changes in the blood following splenectomy which tend to show that basophilic granules in the erythrocytes are derived from the nucleus and are, therefore, indicative of regeneration of the blood. Two days after removal of the spleen, with red cells, 2,350,000, and hemoglobin, 44 per cent., normoblasts became very numerous in the patient's blood. Evenly distributed in the cytoplasm were numerous granules which were stained a blackish blue with Giemsa's stain. The cytoplasm of these normoblasts was orthochromatic. The granules were found only in the normoblasts—none were observed in non-nucleated cells. This fact the author points out, suggests very strongly a nuclear origin of the granules. Since the basophilic granules were present only in young cells in this instance, it is unlikely that they represent degenerative changes.

Lordotic Albuminuria and the Acidity of the Urine.—E. FRAENKEL (*Deutsch. med. Woch.*, 1912, xxviii, 1974) has examined the relationship between lordotic albuminuria and urinary acidity as determined by titration with tenth normal sodium hydrate, using phenolphthalein as indicator. In some cases the albuminuria was induced by having the patients assume the lordotic posture in a chair for fifteen minutes. In many of the children, an increase in urinary acidity occurred with the appearance of albumin in the urine or with the augmentation of a preëxisting albuminuria brought on by the lordotic position; in others, the acidity rose several hours after the albumin appeared. It was possible to suppress the albuminuria by previous administration of sodium bicarbonate, thus supporting Fisher's views. However, in a child whose condition corresponded to lordotic albuminuria following scarlatinal nephritis, as well as in scarlatinal nephritis itself, the administration of alkali was without effect.

Insect Transmission of the Virus of Poliomyelitis.—HOWARD and CLARK (*Jour. Exper. Med.*, 1912, xvi, 850) have experimented with the house fly, certain types of mosquitoes, the bedbug, and head and

body lice, with reference to their ability to carry the poliomyelitic virus. The insects were allowed to feed directly on infected cord or upon materials containing a suspension of infected cord. They were then killed at varying intervals and used whole, or in part, for the preparation of bacteria-free Berkefeld filtrates, which were inoculated into monkeys. Biting insects were made to feed upon monkeys inoculated with poliomyelitic virus and their bodies used in turn for inoculation. The experiments allow these deductions: The domestic fly may become contaminated with the virus which it may obtain in nature from infected discharges from the nose and throat or intestine. The virus can be transported in a living state on the surface of their bodies for two or more days, and within the esophagus and stomach for at least several hours. The virus may be deposited at a considerable distance from the point of contamination. The flies may die, and the disintegration of their bodies may liberate surviving virus in dust. Through such a passive contaminator as the house fly, the bodies may easily be taken into the bodies of human beings. At least two species of mosquitoes are excluded. The pediculi also seem incapable of taking virus out of the blood, or maintaining it in a living state within their bodies. In one of the sixteen experiments with bedbugs, it was shown possible for a blood-sucking insect both to obtain living virus from the blood and maintain it in a living state for at least seven days.

The Bacteriology and Chemistry of the Bile in Vivo, Together with a Method for the Early Diagnosis of Typhoid Fever.—G. KIRALYFI (*Berlin. klin. Woch.*, 1912, xlix, 1985) has made bacteriological and chemical studies of the bile, with particular reference to affections of the gall-bladder. His method is practically the same as that used by Petry (1911) in an examination of the microscopic elements of the bile. The patient is given Boldyreff's oil breakfast consisting of 250 c.c. to 300 c.c. of olive oil; the stomach is, however, first washed with sterile water through a sterile tube, after which the oil is introduced through the tube. After one-half hour, the stomach contents are removed with a sterile tube. The patient is instructed to expectorate all sputum and saliva during the half hour the oil remains in the stomach; in fact, it is essential that nothing be swallowed. The stomach contents are received into a sterile dish. In a few minutes the oil separates above the bile-stained fluid, which has entered the stomach. By means of a sterile pipette, some of the fluid is transferred to tubes of agar and bouillon. The remainder of the bile-stained fluid is used for microscopic and chemical examination. The main object of the study was the bacteriology of the bile in cholecystitis. For purposes of orientation, various diseases were included. In all, 69 patients were examined. In 39 instances, the bile-stained fluid was sterile, showing that the technique employed was successful in preventing the entrance of mouth organisms. In 7 of 8 cases of cholecystitis, the author obtained positive results; the colon bacillus was found four times, the streptococcus once, and staphylococci twice. The sterile fluid was obtained from a patient whose clinical symptoms were mild. In cholelithiasis, the bile was usually sterile. This result Kiralyfi believes was due in part to mechanical interference with

the flow of bile from the gall-bladder, in part to the fact that in a certain percentage of cases gallstones are independent of bacterial invasion. In subacidity and anacidity, the gastric flora may interfere with the bacteriological examination of the bile; this difficulty is not encountered in hyperacidity or normal acidity. In 3 cases of typhoid fever, pure cultures of the *Bacillus typhosus* were obtained from the bile. This result was especially important, for in 2 of the patients cultures of the blood and feces were negative, and the Widal reaction also remained negative. Normal bile contains no albumin. In testing for albumin, material remaining in the stomach was excluded by the lavage, and, as a further check, the wash water was tested. The sulfosalicylic acid test was used for albumin. A positive reaction was obtained in all of the cases of cholecystitis in which bacteria were found; the two conditions run parallel. A trace of albumin (mucin, etc.) is to be disregarded. In cases where there is a strongly marked reaction for albumin with negative culture, the possibility of a latent or masked cholecystitis without symptoms must be considered. Microscopic examination of the bile is not of great value. One or two pus cells are without significance. It is only when the cells are abundant that their presence points to an inflammatory exudate. The albumin may be increased regardless of the number of pus cells.

Alimentary Galactosuria in Liver Disease.—E. REISS and W. JEHN (*Deutsch. Archiv f. klin. Med.*, 1912, cviii, 187) find that galactose is superior to levulose in some respects as a measure of hepatic function. Galactose was first used in hepatic diagnosis by Bauer in 1908. The authors have administered 40 grams of galactose in the morning on a fasting stomach, as Bauer did, after the patient has voided urine. The sugar is best taken in a carbonated water. An hour after taking the galactose, the patient may have his breakfast. (If the patient has diarrhea or is vomiting, the test should be delayed; the authors have never seen either of these symptoms as a sequel of giving the sugar.) The urine is collected for twelve hours, in two six-hour periods. The greater part of the sugar—usually all—is eliminated in the first six hours. After twelve hours, none is excreted. The urine is tested qualitatively with Nylander's and Trommer's tests, quantitatively with the polariscope or by titration. In normal individuals and in those in whom liver disease could be excluded, 1.5 gram at most was recovered—usually none, though it must be added that one neurasthenic excreted 2.5 gram. The authors consider amounts pathological only when they exceed 2 grams. The authors have employed the test in more than 100 patients with liver disease and have found, as did Bauer, that alimentary galactosuria is unusual in many diseases of the liver. Thus, in cholelithiasis it was usually found that galactose was excreted in normal amounts. Obstruction of the bile passages by tumors never led to galactosuria. Luetic icterus (secondary stage) gave negative results in 3 cases, moderate galactosuria (2 to 4 grams) in 2 cases. Of 8 cases of chronic passive congestion, only 1 showed a moderate galactosuria. Fifteen cases of cirrhosis of the liver were studied. In the majority the tolerance for galactose was normal; in only 3 cases was a moderate galactosuria found. Among 17 cases of catarrhal jaundice, only 1 very mild case failed to show galactosuria.

The galactose was usually excreted in moderate or large amounts, as much as 36 per cent. of the quantity given being recovered. Of other conditions, only 1 case of croupous pneumonia showed galactosuria, other cases of this disease being negative. Thus, a normal tolerance for galactose speaks against catarrhal jaundice alone; it may be found in all other hepatic conditions. (The authors have had no opportunity to study acute yellow atrophy and phosphorus poisoning, but believe a galactosuria will be found in these conditions.) Similarly, in the absence of febrile disease, marked galactosuria indicates catarrhal jaundice, or possibly one of the two conditions mentioned above. Moderate galactosuria may occur in most diseases of the liver. It is lacking in cancer and is rare with cholelithiasis and chronic passive congestion.

Carcinoma Skin Reaction.—The relation of the skin reaction for carcinoma proposed by Elsberg, Neuhof, and Geist to the isohemolysin classification (Moss) has been shown not to be a matter of indifference. There appears to be one group, Group IV (the corpuscles of which are neither agglutinated nor hemolyzed by any serum in vitro) which might be utilized for the reaction with reasonable reliability, since when these corpuscles have been hemolyzed, hemolysis of those of the other three groups has always occurred. This fact demonstrated by Gorham and Lisser has led LISSER and BLOOMFIELD (*Johns Hopkins Hosp. Bull.*, 1912, xxiii, 356) to test a series of cases, making use of only the corpuscles of Group IV. They studied 62 verified cases of carcinoma and sarcoma and 94 cases of healthy individuals or patients suffering from non-malignant ailments. Two-thirds of the malignant cases gave a positive reaction. In the control cases 91.6 per cent. were negative. They concluded that a negative skin reaction adds little or no weight to the evidence against cancer. But a positive reaction is strong presumptive evidence of cancer. They believe the corpuscles of Group IV must be used to give reliable results.

Nitrogen Retention in the Blood in Experimental Acute Nephritis.—FOLIN, KARSNER, and DENIS (*Jour. Exper. Med.*, 1912, xvi, 789) following the development of colorimetric methods of nitrogen determinations in the blood, studied the possible nitrogen retention in experimentally produced nephritis. The types of nephritis selected were those produced by uranium nitrate, by potassium chromate, and by cantharidin. In the uranium nephritis, which involves both tubules and glomeruli, the former more markedly than the latter, a marked accumulation of nitrogen occurs in the blood. Chromate nephritis, involving tubules almost exclusively, results in only moderate nitrogen retention. Cantharidin causes a nephritis of both tubules and glomeruli, especially the latter, and in this type there is produced a marked early and persisting accumulation of nitrogen. It must be noticed that the glomerulus is distinctly involved in the two forms where accumulation of nitrogen in the blood is most marked, a condition indicating that although almost pure tubular involvement produces only moderate accumulation, the additional involvement of the glomerulus is extremely important in leading to a retention of nitrogenous waste products.

SURGERY

UNDER THE CHARGE OF

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Anesthesia of the Sciatic Nerve.—BABITZKI (*Zentralbl. f. Chir.*, 1913, xl, 227) says that for successful anesthetization the injection must be intraneural. Paraneural injections are extremely unreliable. In the best cases the anesthesia may be insufficient and in the worst we risk the development of general toxic symptoms before the occurrence of the anesthesia. Paraneural injections of salt solutions in large quantities, give good results in sciatica. Although much of the fluid is absorbed there still remains a considerable quantity in a compact layer pressing on the nerve. It is otherwise with a toxic anesthetizing fluid. Novocain solution (2 to 3 or even 4 per cent.) must be economically employed. Babitzki uses the following method: The finger in the rectum reaches to the point where the nerve bends over the edge of the great sciatic foramen to pass downward in the groove between the tuberosity of the ischium and great trochanter. The great sciatic foramen is formed from the great sciatic notch by the great sciatic ligament passing from the sacrum to the spine of the ischium. The spine of the ischium is easily found by the finger which is then made to press upon the bone and ligament in the whole circumference of the foramen carrying the contents of the foramen before it. The nerve is almost entirely covered by the pyriformis muscle and only a small portion of it lies below the margin of this muscle between it and the bony edge of the foramen. The injection needle is introduced, under the control of the finger in the rectum, through the gluteal muscles down to the foramen, and the needle point can be made to find any desired portion of the thick nerve trunk. It is of the greatest importance that the nerve itself can always be found. When the nerve is injected the result develops rapidly within a few minutes—not in the course of an hour or half an hour (Jassentzki and Wojno). The method has been employed in 15 cases, in which the results were completely satisfactory. It was used for amputation of the femur, Madelung's venesection, inflammatory process of the foot bones, fractures of the femur and bones of the leg, as well as for sciatica. About 5 c.c. of a 3 per cent. solution of novocain is first injected into the anterior crural nerve, by Lawen's method, when the patient is turned face downward. The fractures gave most difficulty, for which the necessary precautions must be taken. The

patient usually will have had applied first aid to the injured dressing, which should not be removed until after the injection is made. The technique and the rules of asepsis for the manipulations in the rectum are generally known.

Subcutaneous Rupture of the Diaphragm and Positive Pressure (Meltzer).—RIEBEL (*Surg. Gynec. and Obst.*, 1913, xvi, 133) made a study of the literature after an experience with a case of rupture of the diaphragm in a boy, aged ten years, who had a wagon loaded with gasoline cans pass over his left leg and side of chest, the boy lying prone on the ground. Operation showed the entire stomach in the pleural cavity and the entire left half of the diaphragm, as far back as the costal angle, detached from the ribs at right angles to its fibers. Inspection revealed the stomach and intestines as well as parenchymatous organs uninjured. A postmortem was not held. From his study Riebel concludes that the diaphragm has an important influence upon the heart's action, by its anatomical relation to the heart and pericardium. It is an important factor in the circulation by aiding the venous return, especially from the abdominal cavity. It plays an important part in maintaining equilibrium in the thoracic cavity. Rupture of the diaphragm must needs be followed by serious disturbances in respiration and in the equilibrium within the thoracic cavity. The inevitable prolapse of abdominal organs following subcutaneous rupture still increases this condition, frequently producing a state of positive pressure in the thoracic cavity. The use of differential pressure is absolutely necessary to overcome these factors. It will insure better results, in these cases, permitting, furthermore, the choice of abdominal or pleural route or both as the occasion requires. The character of pressure, whether positive or negative, is of little consequence, but the method of Meltzer is simple and can be used anywhere. In cases of suspected subcutaneous rupture of the diaphragm, insufflation should be employed with low pressure (10 to 15 mm.) before operation, to overcome the deleterious effects of disturbed intrathoracic equilibrium.

A Case of Extensive Subcutaneous Emphysema Following Intratracheal Anesthesia, with Recovery.—LUKE (*Surg. Gynec. and Obst.*, 1913, xvi, 204) reports the case of a woman, aged thirty-six years, operated on for a decompression under intratracheal insufflation, for a cerebral tumor. The patient was placed in the prone position, with the head strongly flexed over the end of the table, which proved to be a bad position for breathing and for managing the giving of the anesthetic. The color and pulse were entirely satisfactory for the first ten minutes. During the next twenty-five minutes there was a moderate cyanosis occasionally which was relieved by extending the head a little. About ten minutes later the blood in the wound was noted to be very dark and the face was cyanosed and generally swollen, especially on the left side. The intratracheal tube was withdrawn without a moment's delay and the patient quickly turned to the dorsal position and artificial respiration begun. There was also a marked swelling as far as the umbilicus, anteriorly, and to the base of the spine posteriorly, all of which gave the characteristic crackle, on palpation, of subcutaneous emphysema. The decompression operation

was performed after some improvement in the condition of the patient, under a very small amount of drop ether. The patient recovered to die from a later operation for the removal of the tumor. The following possibilities are considered in explanation of this accident: (1) That of the direct trauma due to the catheter either during introduction or afterward; again from pressure of the long narrow sand bags under the neck. (2) Trauma brought about by overdistention: Here is considered the possibility of inserting the catheter too far, and thereby plugging tightly a bronchus, leading to overdistention and rupture of the lung. In this case perhaps obstruction was possible from the extreme flexion and pressure of the sand bags beneath the neck. Again the catheter may have been too large (No. 24 was used), but from experience this seems unlikely. This is the second accident of this kind in New York City during the use of this method. The other case resulted in death and was thought to be due to the catheter slipping into a bronchus and plugging it, with consequent excessive distention and rupture of the lung. It is admitted that errors in technique may have been entirely responsible for this accident; but it teaches the valuable lesson that the method is not entirely without danger, and, further, that a safety device (which was not applied to the apparatus in either of the above cases) which will efficiently guard against high intrapulmonary pressure, is absolutely essential.

Treatment of Wounds of the Venous Sinuses of the Cranium.—AUVRAY (*Arch. gén. d. chir.*, 1913, lvi, 257) collected from the literature 163 cases of wounds of the superior longitudinal and lateral sinuses and reports 3 new cases. He emphasizes the gravity of the prognosis and studied the various therapeutic procedures and their comparative value. He discusses the employment of sutures, of forceps which are left in position, of the lateral and circular ligature, and of the tampon. The latter is the oldest of all and in Auvray's statistics was employed in 75 out of 112 cases operated on. In 9 other cases the method of hemostasis was not indicated. In favor of the tampon are its simplicity, the rapidity with which it can be applied, and its great efficacy. Even when the suture or forceps pressure is employed, the tampon serves as a complimentary method, and renders more perfect the hemostasis of the venous wound. The necessity of leaving the wound open exposes the patient to the danger of the introduction of infectious material and the development of phlebitis which was common in the earlier cases. But the present-day use of sterile and antiseptic gauze, as iodoform gauze, makes these complications little to be feared. Another objection raised against the tampon is the danger of pressure by it upon the brain. Auvray did not experience this complication in any of his cases, and believes that it will be of minimal importance in any case, since it can be obviated at any time by the removal of the tampon. He maintains that the superiority of the tampon over all other methods is incontestable.

THERAPEUTICS

UNDER THE CHARGE OF

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Further Observations on the Treatment of Human Cancer with Intravenous Injections of Colloidal Copper.—LOEB, LYON, McCLURG, and SWEET (*Interstate Med. Jour.*, 1913, xx, 9) report a further series of 19 cases of human cancer treated with repeated injections of colloidal copper. Rapidly growing tumors which lead to extensive metastases in the internal organs are not amenable to this treatment. In a large number of cases the effect of the injections gradually decrease. This method, however, causes a gradual although partial retrogression of the large majority of inoperable cancers, provided they have not reached the final stage of the disease. However, they believe that the method is too slow in its action to render probable a cure except in a few cases. They say in addition that it is too early to predict the ultimate fate of the patients who are now under treatment.

Pneumothorax Treatment of Pulmonary Tuberculosis.—V. JAGIÉ (*Wein. med. Woch.*, 1913, lxiii, 379) gives the following as necessary conditions before inducing artificial pneumothorax for therapeutic purposes: (1) Good motility of the chest wall that above all should not be adherent to the apex of the lung. Adhesions at the base do not prevent the desired compression of the diseased lung. Pain during the injection is a symptom of the presence of adhesions. (2) It is necessary that the cavity walls be thin and compressible. If the walls are fixed the method is of no use. (3) A good heart action. The author says that this therapy is especially indicated when there are a number of cavities of greater or smaller size on one side with few adhesions, and on the other side only slight infiltration or an apical lesion. The treatment is also indicated in any disseminated unilateral tuberculosis. Persistent hemoptysis is also an indication when one knows the bleeding side. Jagié has also seen good results obtained in tuberculosis of the larynx where the benefit derived was probably due to its good effect upon the cough. Intestinal tuberculosis and amyloid degeneration are contraindications to the treatment. Tuberculous pleurisy is a problematical indication for the treatment. The best age for the treatment is from fifteen to thirty-five years, but this procedure can also be utilized in tuberculosis of children.

Benzol Treatment of Leukemia.—NEUMANN (*Therapie d. Gegenwart*, 1913, liv, 56) reports a case of leukemia that improved remarkably after a course of thirty-six days' treatment with benzol. He followed Koranyi's directions, giving at first one 0.5 gm. capsule of benzol twice a day and increasing the dose to two capsules of 0.5 gm. each four times a day. Soon after the end of the benzol course the patient

developed fever and diarrhea, with repeated epistaxis and hemorrhagic stomatitis and rhinitis, and died thirty-nine days after the discontinuance of the benzol. Neumann states that the bone-marrow findings resembled those found by Selling in benzol-poisoned rabbits. The benzol used is not specified by Neumann, and Selling thought that the toxic action of the benzol used in his experiments was probably due to anilin present in the benzol as an impurity. Neumann believes that benzol is a very effectual remedy for leukemia, but its use requires great caution. He thinks that it should be discontinued as soon as a distinct tendency to improvement begins.

The Emetin Treatment of Amebic Dysentery.—ALLAN (*Jour. Amer. Med. Assoc.*, 1913, lx, 664) says that for a number of years, English physicians working in India have maintained that ipecac is the best remedy for amebic dysentery, and within the past few years the American profession has largely come to agree with them. In March, 1911, Vedder, working in Manila, published his findings that a fluid extract of ipecac would kill amebæ in cultures in dilutions as high as 1 to 200,000. The next year Rogers in Calcutta found that emetin hydrochlorid killed amebæ in stools in dilutions of 1 to 100,000 and began the use of this salt hypodermically in cases of amebic dysentery. His brilliant results led Allan to try this method of treatment and he reports two cases of amebic dysentery in detail that were promptly cured by subcutaneous injections of emetin hydrochlorid.

Induced Pneumothorax in the Treatment of Pulmonary Disease.—HAMMAN and SLOAN (*Bull. Johns Hopkins Hosp.*, 1913, xxiv, 53) describe the history of the production of artificial pneumothorax for the treatment of pulmonary tuberculosis, the proper selection of cases for this treatment, the different methods, of which two are mainly in use, Brauer's method by incision down to the pleura and Forlanini's puncture method. Hamman and Sloan prefer the latter method. They give in detail their method of inducing pneumothorax. The chief dangers attending induced pneumothorax are two—infection and air embolism. Air embolism is the more important complication and has followed attempts to produce pneumothorax only upon the injection of gas in the absence of satisfactory evidence that the needle is in the pleural cavity. The whole procedure of producing and maintaining pneumothorax should be guided by the manometer, and the authors give very valuable data regarding the information given by the manometer. Hamman and Sloan's conclusions are as follows: (1) Induced pneumothorax is a harmless procedure and the operation, carefully performed, is without danger. (2) In 3 out of 20 cases it was impossible to produce any pulmonary collapse owing to general pleural adhesions. (3) Of 16 cases in which pneumothorax was successfully produced in but 7 was the pneumothorax complete. (4) Of 9 cases with induced pneumothorax existing for four months or longer, 4 have developed pleurisy with effusion. (5) The pneumothorax has, in most instances, an immediate and striking influence upon the cough and expectoration, tubercle bacilli may disappear from the sputum. (6) Constitutional symptoms abate more slowly. In most instances there is at first a loss in weight followed by a gradual

rise. (7) The total collapse of one lung causes surprisingly little inconvenience. Usually there is but slight dyspnea on exertion. Many of the patients with an induced pneumothorax assist actively in the work about the sanatorium. (8) The procedure is of great value in the treatment of pulmonary hemorrhage. (9) While induced pneumothorax will never become a routine method for the treatment of pulmonary tuberculosis, still in selected cases it offers a prospect of temporary and permanent relief when the usual methods of treatment have been unsuccessfully tried. Quiescent lesions in one lung with acute recrudescence in the other are the most favorable for the treatment. Its use need by no means be limited to strictly unilateral lesions, but when there is advanced disease of both lungs little benefit can be expected. It would seem advisable not to withhold the treatment until the patient is hopelessly advanced, but to apply it judiciously to suitable moderately advanced patients in whom the disease tends to progress in spite of appropriate treatment. The article is a valuable one and should be consulted for details of the procedure.

Experiences with Induced Pneumothorax.—VAN DEN BERGH, DE YOUNG and SCHUT (*Beiträge z. klin. d. Tuberkulose*, 1913, xxvi, 47) report 13 cases where pneumothorax was produced for therapeutic purposes in pulmonary tuberculosis. They believe that this procedure should be restricted to cases of severe pulmonary tuberculosis when the lesion is chiefly or entirely unilateral and should be used in these cases only when the ordinary methods of treatment have failed to benefit. There is danger of increasing or making more active a slight tuberculosis of the opposite side and this danger must be taken into consideration. This result occurred in some of the cases reported, and in 2 it was confirmed by autopsy. The direct dangers of the operation, chiefly air embolism and injuries to the lung, are very slight with good technique. A marked effusion should be partly withdrawn before inducing pneumothorax or afterward, in maintaining the pneumothorax. An artificial pneumothorax should only be induced by an expert, preferably in a hospital where advantage may be taken of Röntgen-ray examinations. As to the choice of methods for producing the pneumothorax they believe that the puncture method of Forlanini should have the preference over the incision method of Brauer.

Benzol in Leukemia.—WACHTEL (*Deutsch. Med. Woch.*, 1913, xxxix, 307) reports 2 cases of leukemia where he gave benzol. The first was a case of severe myeloid leukemia and he was obliged to stop the benzol after the third day, as albumin appeared in the urine. The second case showed marked improvement under 3 gm. of benzol given daily. In the first two weeks the improvement was apparent only in a return to a normal temperature and an improved general condition. In the fourth week the leukocytes dropped from 102,000 to 37,000. In the first three weeks the mononuclears predominated, but after this the myelocytes decreased and the polynuclears increased, and the spleen returned to normal size. A blood examination made four weeks after the benzol had been discontinued showed a hemoglobin percentage of 78; red blood cells, 4,200,000; white blood cells,

8,000, of which 80 per cent. were polynuclear neutrophiles, 12 per cent. lymphocytes, and 2 per cent. each of eosinophilic and neutrophilic myelocytes. The fact that the hemoglobin percentage and the number of reds increased while under the benzol treatment is especially noteworthy.

PEDIATRICS

UNDER THE CHARGE OF

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Tuberculous Infection in Children.—ARMT DE BESCHE (*Deutsch. med. Woch.*, 1913, xxxix, 452) reports an interesting investigation to determine the percentage of tuberculous infection in children. Lymphatic tissue from the mesenteric, bronchial, and cervical glands of 134 children coming to autopsy was injected into guinea-pigs and rabbits, and the results studied and followed out. In 28 of these children tuberculosis was the cause of death. In 14 it was discovered, latent at autopsy. In 10 cases only "latent bacilli" were found in the lymphatic glands. Tuberculous infection was proved in 52 of the 134 children. The percentage of infection rose proportionately with the age period, from one to fifteen years. In the greater percentage of lymphatic tuberculosis the condition was found widespread and general throughout the body. In 45 of the positive cases the bacillus was found to be of the human type, proving that the greater majority of tuberculous children receive the infection from human beings. In 3 cases the bovine type of bacillus was isolated, and 1 case showed both the human and bovine type. This investigation was made in the city of Christiania, and apparently shows that from 6 to 8 per cent. of tuberculous infection in children comes from cows and the balance from human beings.

Length of the Incubation Period in Infantile Paralysis.—CARL SCHOU (*Deutsch. med. Woch.*, 1913, xxxix, 493) determined the average incubation period in an epidemic of anterior poliomyelitis in Sweden. He also attempted to trace the method of infection, especially in two families, closely associated, in which 6 children were afflicted. From his series of cases Schou determines the average period of incubation to be about four days. As the infectious element exists in the blood as well as in the secretion from mucous membranes, the transmission of the disease is made possible through blood-sucking insects as well as directly or indirectly from person to person by infected secretions. In Sweden a large number of cases occur in winter, when the stinging fly is not in evidence. To accuse the fly, therefore, one would have to assume a very long incubation period. His investigations do not point to blood-sucking insects for the dissemination of the disease, nor did it seem probable that the horse-fly could have caused the

infection of such a large number of people in two families, from the original case afflicted with that disease. It seems much more likely that the infectious secretions of the nose and mouth from the original case directly or indirectly infected the other members of the families.

Effect on the Child of Salvarsan given to the Syphilitic Mother.—MARIE HOLTH (*Deutsch. med. Woch.*, 1913, xxxix, 462) reports 9 cases in which pregnant women with syphilis were given salvarsan with most beneficial effect on the subsequent condition of the children. In only 2 of these cases were there any syphilitic symptoms in the children, who were under observation from ten weeks to one year after birth. The majority of these women received the treatment during pregnancy. Some had given birth during the previous two years to syphilitic infants. In 7 of the cases no syphilitic symptoms developed in the child. One woman was given the treatment while nursing a congenitally syphilitic child. Through the mother's milk the child received the benefit of the treatment also, and the syphilitic signs disappeared and it developed normally. These cases show that this treatment of the mother or the prospective mother exerts a very favorable influence on the vitality and development of the child.

The Mental Defective and Society.—WILLIAM LELAND STOWELL (*Archives of Pediatrics*, 1913, xxx, 203), after describing the condition known as defective or feeble-minded, gives the number of feeble-minded individuals in the United States as more than 300,000. In New York State there are 30,000, of which less than 4000 are in institutions. Special classes for defective children, separating the abnormal from the normal and giving them work according to their needs, is primarily approved of. The practical outcome of this fine work is criticised because a subnormal child should be in an institution all the time, not a public school a short time. Scarcely one-tenth of the children ever rise to the normal grades. All feeble-minded individuals should be segregated in public or private institutions. This applies especially to feeble-minded girls and women because of their lack of moral force. In 300 families containing mental defectives there were 2013 children born, 434 of which were defective and 160 criminal or pauper. Statistics are abundant and experience the same everywhere. In several homes for prostitutes as high as one-third were found to be feeble-minded. The possibility of procreation is the most vital factor in the large class of feeble-minded. Feeble-mindedness is an incurable condition, not a disease. Out of 341 patients discharged from an institution, 85.5 per cent. were subsequently found to be absolutely useless, and should have been taken care of for life. Preventive measures in the form of sterilization for all feeble-minded not segregated should be required by law, to avoid the multiplication of this unfortunate class.

Practical Points in the Management of Breast Feeding.—ERIC PRITCHARD (*Archives of Pediatrics*, 1913, xxx, 164) deprecates the lack of attention and study given to breast feeding by pediatricists and obstetricians. He calls attention to the common mistakes made in the management of breast-feeding, especially during the first weeks

of life. First and most serious of mistakes is to give the infant the usual dose of castor oil. The meconium supplied by nature acts as an intestinal lubricant and offers sufficient stimulus to the nerve centres regulating defecation. Castor oil overstimulates these nerve centres, dislocating their automatic functions. The delicate epithelial lining of the intestinal canal is injured by the oil, which sweeps out the meconium and tears off shreds of mucous membrane. Meconium is so important to the bowel that where it is deficient Pritchard replaces it by petroleum emulsion, the best substitute known to him. It is protective, lubricant, and soothing. The incidence of thrush in infants is often due to loss of epithelium from cleansing the mouth of the infant with a clean rag to render it aseptic. Preserving the continuity of the epithelium will keep the mouth more healthy than cleansing with a linen rag. Another point of greatest importance is the management of the number of feedings. Pritchard claims better results from three- or four-hour intervals between feedings than from the usual method of two-hour intervals. This gives a long interval of rest between feedings. If the quantity of breast milk is insufficient for this long interval it should be supplemented by a feeding of appropriate food immediately after the breast. Pritchard voices a distrust of the caloric method of infant feeding. The quantity of food should be estimated by a "test feed," and if below the normal standard a supplementary feeding should be begun. A "test feed" consists of weighing an infant three hours after its last breast feeding, then putting it to the breast for a regular feeding, and weighing the child immediately afterward to determine the quantity of food taken. Infants too often do not obtain progressively larger quantities of milk as they grow older. The supply of breast milk will vary with the hygienic environment of the child. The "test feed" applied systematically shows that London children at least secure an amount of breast milk enormously below the usually accepted estimates. This suggests modifications in the method of breast feeding and of artificial feeding. An infant requires time to learn to digest a new food. New foods therefore should be given at first in very small amounts or in a predigested form.

Some Cases of Jaundice in Childhood.—F. J. POYNTON (*British Jour. Child. Diseases*, 1913, x, 145) discusses several types of jaundice occurring in infancy in which diagnosis is difficult. He cited 3 cases in which the jaundice appeared during the first four days of life. These cases showed moderate jaundice, liver enlarged, but not hard, stools white and undigested, but no enlargement of the spleen. At times bile appeared slightly in the stools and the jaundice and the size of the liver diminished slightly. These cases recovered gradually in from seven to twelve months. They were never breast fed. They are clearly obstructive cases, and not of the same nature as acholuric jaundice, or *icterus neonatorum*. Poynton suggests an unusually viscid bile as a possible cause. The treatment and feeding of these cases is difficult. Fats are not tolerated and nutrition is diminished. Foods used successfully by Poynton include malted milk, Walker-Gordon modified milk with low fats, raw meat juice, and brandy. Among drugs the most serviceable were small doses of gray powder,

and bicarbonate and salicylate of soda. The second type of jaundice is known as congenital, family, periodic jaundice in which the disease runs in families and shows an acholuric jaundice with enlargement of the liver and spleen, and anemia of varying degree. The blood shows fragility and reticulation of the red cells. Jaundice may disappear temporarily with the development of grave anemia and a large, hard spleen. Severe recurrent pain over the spleen and epigastrium is rather characteristic. The third type of jaundice is syphilitic in origin. Three cases are reported in children, aged seven, nine, and ten years. There was a history of "fits" or epileptiform attacks in all of them. The first two cases had enlarged livers with intense jaundice and bile in the urine, and ascites. They developed chronic meningitis and succumbed. Both showed parenchymatous changes in the liver and endarteritis. The third case developed jaundice, pale stools, and enlarged liver, but on antisiphilitic treatment recovered and ultimately developed fairly well mentally and physically. The Wassermann reaction should be of assistance in diagnosing this type.

GYNECOLOGY

UNDER THE CHARGE OF

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Nervous Sequelæ of the Artificial Menopause.—A considerable series of clinical investigations have been carried out by MOSBACHER and MEYER (*Monatschr. f. Geb. u. Gyn.*, 1913, xxxvii, 337) to determine if the nervous phenomena, which are commonly supposed to follow the artificial menopause, have a basis in demonstrable physical changes in the organism. One of their chief lines of investigation was to determine if the theories of Schiekele (recently discussed in this department) with regard to the blood-pressure reducing action of the internal secretion of the ovary could be demonstrated clinically. For this purpose they have tested before and at varying periods after operation the blood pressure of 67 women who were subjected to double oöphorectomy, considering a rise or fall to have taken place only when the readings varied by 10 mm. or more—Sahli instruments. They found after operation a rise in 13 and a fall in 17 cases; in 7 of the former and in 9 of the latter marked nervous disturbances were present; in the other patients these were lacking. Mosbacher and Meyer conclude, therefore, that the blood pressure cannot be considered in any way dependent upon the presence or absence of ovarian secretion, nor can the occurrence of nervous phenomena be considered a result of blood-pressure changes; they have thus been entirely unable to confirm clinically Schiekele's physiological experiments, or to demonstrate such an antagonism between the ovarian and adrenal secretions as he believed to exist. Tests directed to ascertaining

whether any increased stimulation of the sympathetic nervous system occurs after castration, as evidenced by a change in the amount of adrenalin necessary to produce glycosuria when introduced subcutaneously, or of cocaine to produce mydriasis when dropped into the eye in very weak solution, produced likewise totally inconstant results, from which no definite conclusions could be drawn. As a result of these investigations, and of clinical observations in general, Mosbacher and Meyer express themselves as being extremely skeptical with regard to the existence of any causal relation whatever between operative castration and the occurrence of definite nervous disturbances, believing that most of these which do occur, apparently as a result of operation, are in reality manifestations of psychoneuroses which have little or nothing to do with removal of the ovaries. In substantiation of this contention they quote a few instances of women, upon whom no operation had been performed, and whose internal genitalia were entirely normal, but who presented to a marked degree all the typical symptoms usually ascribed to the artificial menopause. They also found that a considerable number of patients complaining after oöphorectomy of hot flashes, attacks of sweating, palpitation of the heart, etc., had also been troubled with the same conditions before operation, whereas in other cases symptoms of this nature which had existed before operation disappeared after it. With regard to the occurrence of postoperative disturbances of a more psychic nature, such as mental depression, anxiety, irritability, Mosbacher and Meyer claim that all patients complaining of these admitted the presence of "nervousness" beforehand, entirely new symptoms occurring only in very occasional instances.

Acute Tuberculosis following Gynecological Operations.—A number of quite remarkable cases are reported by PROCHOWNIK (*Zentralbl. f. Gyn.*, 1913, xxxvii, 7) to illustrate the possibility of the occurrence of rapidly spreading acute tuberculosis, leading to a fatal termination, in individuals in whom there was not the slightest suspicion of a tuberculous infection, the immediate causative factor in most of these being some apparently trivial operative procedure. The salient features of the most instructive of these cases are, very briefly, as follows: (1) Curettement for dysmenorrhea and irregular bleeding. Entirely well up to the ninth day, then suddenly high, remittent fever. Lungs and pleura free until ten days before death, which occurred in a very few weeks. Autopsy: Miliary tuberculosis arising from uterus and right tube; tubercles over entire peritoneum; fresh miliary foci in lungs and pleura. (2) Reposition of retrodisplaced uterus (narcosis). Well up to seventh day, then high, remittent fever. Death in eleventh week. Autopsy: general abdominal tuberculosis; moderate involvement of lungs and pleura. Origin, a tuberculous focus in right tube, which had been torn loose from the rectum by the forced reposition of the uterus. (3) Forced reposition of a retrodisplaced uterus by means of the sound (narcosis). Following this, a parametric abscess formed, which was opened and drained. Wound healed, but high, remittent fever came on, and lasted for four and one-half months; lung involvement only in last two weeks. Autopsy: acute miliary tuberculosis in abdomen; fresh foci in lungs; origin

from right tube. (4) Abortion (self-induced), curettement; death on forty-eighth day. Autopsy: tuberculosis of both tubes, miliary tuberculosis of entire peritoneum; small, recent foci in lungs and pleura. (5) Double salpingectomy for gonorrheal pyosalpinx (gonococci demonstrated in the pus). Death on the forty-ninth day. Autopsy: extensive peritoneal tuberculosis; no involvement of lungs; few tubercles in pleura. In none of these women was there the slightest reason to suspect the presence of a tuberculous focus anywhere, except that the husband of one was known to be tuberculous, and in two of the others this was suspected. The patients themselves were all in good health, except for the condition for which the operation was performed, and in none did repeated examinations of the lungs by trained internists reveal any signs of trouble until shortly before the end. While Prochownik admits that cases of this sort are fortunately extremely rare—the ones reported are culled from an experience of many years—the fact that they may occasionally occur should be a warning, he thinks, to the utmost caution in dealing with all cases in which there is even the possibility of a tuberculous infection of the genital tract, since they prove the fallaciousness of Krönig's commonly accepted dictum, to the effect that "genital tuberculosis leads extremely rarely to miliary tuberculosis, and practically never causes, either directly or indirectly, the death of the individual."

DERMATOLOGY

UNDER THE CHARGE OF

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Industrial Skin Diseases.—KARL HERXHEIMER (*Deutsch. Med. Woch.*, January 4, 1912) refers to seventy-four means through which chronic eezema may be acquired. Industrial acne, vaccinia in milkers, furuncle in workers with cement, ulcers from glass, sand, and dust, and workers in chromium salts are mentioned. Where the tarry products are used, frequent washings of the skin should be resorted to in order to prevent inflammation of the follicles and skin.

Contagious Diseases of the Skin.—J. T. BOWEN (*Boston Med. and Surg. Jour.*, December 14, 1911) directs attention to the common contagious diseases of the skin of frequent occurrence in schools, referring specially to impetigo contagiosa, ringworm, marginated dermatitis of the thighs and axillæ, verrucæ, alopecia areata, and scabies. He urges supervision of the children and young persons in schools and institutions.

Etiology of Leprosy.—WILLIAM TURNER, of Gibraltar (*Brit. Jour. of Derm.*, September, 1911), cites the case of a man, imbecile from birth, an inmate of the Gibraltar lunatic asylum for nineteen years, at the

end of which period he first showed cutaneous lesions on hands and feet, deemed for a year to be syphilitic, but subsequently proved to be leprous. Notwithstanding the usual disfigurement and deformity attending the disease the general health for a number of years remained good. How this man became the subject of leprosy it seemed impossible to discover. No case of leprosy had been known to exist in Gibraltar for thirty years or longer, and the patient had had no communication with the outer world, except at intervals with his sisters who were healthy. A contagious origin in this case seems absolutely untenable. Heredity, insanitary conditions of life, uncleanliness, emanations from the soil, and food supply as possibilities of contagion were likewise not tenable theories. The bacilli of lepra were demonstrated in the lesions of the face. The patient subsequently died from swellings in the mouth and pharynx and exhaustion from lack of being able to partake of nourishment.

Venesection Plus Saline Infusion in Treatment of Skin Diseases.—J. SIMOND (*Deutsch. Med. Woch.*, November 30, 1911) has attained good results by this method in eczema, urticaria, pruritus, and furunculosis, and especially in cases refractory to other methods of treatment. Toxins are washed out by withdrawing 100 to 200 c.c. of blood from a vein and subsequently infusing without removing the canula 300 to 700 c.c. of a 0.9 per cent. salt solution. The operation may be repeated from 3 to 6 times every 5 or 6 days. Simond's experience extended over 100 cases of skin disease.

Salvarsan at the New York Skin and Cancer Hospital.—HOWARD FOX and W. B. TRIMBLE (*Jour. Amer. Med. Assoc.*, November 18, 1911), after eight months' experience, conclude that salvarsan is a powerful symptomatic remedy for the treatment of syphilis; that it acts with greatest rapidity on lesions of the mucous membranes, and further that it is of decided value in obstinate palmar and plantar syphilodermata. It should be used in conjunction with mercurv, and cannot replace this valuable remedy, except in a few selected cases. The effect of the salvarsan on the Wassermann reaction is in general analogous to that of mercury. The intravenous and intramuscular methods of administration are probably of equal efficiency. Where rapidity of action and the comfort of the patient are to be considered the intravenous method is to be chosen.

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